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THE CONTRIBUTIONS OF CHARLES DENISON AND HENRY SEWALL TO MEDICINE[1]

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THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK, N. Y.

IT gives me the greatest pleasure that you have invited me to come home, as it were, to have a share in this ceremony to commemorate two great men and the distinguished services they have rendered to the development of medicine in this community. To those of you who are students in this medical school, the significance of the evening lies in the future, for the dedication of the Charles Denison Memorial Library and the starting of the Henry Sewall Lectureship in Medicine are gifts that mean continuing opportunities for your education. But to those of us who are of an older generation the occasion is crowded with memories.

We who knew Dr. Denison, and indeed you who never saw him, save in the revealing portrait which hangs in the library, recognize him as a physician, as the type that all through the ages has been attracted to medicine. In his portrait one can see his extraordinary kindliness as well as the fact that his most outstanding characteristic was his objectivity. By temperament interested in people, he was the kind of man that the Germans have called a *Menschenfreund*. Beloved of his patients, he carried them through their illnesses. He was trained for medicine in an earlier day, 1867–1869, when observation of the patient was the main method for the diagnosis of disease, yet he was quick to accept the advances of his time. He was inventive and repeatedly published articles on new tools of precision for his work—a new stethoscope, a new spirometer. Skilled in the art of medicine, yet he liked its science. His most absorbing interest was in the therapeutic properties of light. Long before

[1] Address on the occasion of the dedication of the Charles Denison Memorial Library and the inauguration of the Henry Sewall Lectureship in Medicine, University of Colorado School of Medicine and Hospitals, Denver, May 28, 1937.

its use was recognized in the treatment of tuberculosis, he felt that he had cured himself with sunlight. Far ahead of his time, he believed that light and electricity were one and the same, and that the time would come when light would be used and understood in the healing of disease. How he would now enjoy all that has been learned since his time—the use of the x-rays and ultra-violet light!

Having come to Colorado for his health (1873), he turned his attention to tuberculosis and gave up his former work on diseases of the eye and mechanical surgery. His papers show repeatedly that he had marked mechanical skill. He made extensive studies of the use of tuberculin in the treatment of tuberculosis and published several reports of his results. In one I was especially interested because he had had repeated blood counts made after the injections. These counts were made for him by Dr. A. M. Holmes[2] who, as far as I can ascertain, was the first one to find changes in the blood cells in tuberculosis. In 1896 Holmes found that with the advancing disease the neutrophilic leucocytes rise and the small lymphocytes decrease, and the converse with regressing lesions.

Dr. Denison became a profound student of climate, and most of his published work concerns the broad aspects of climate with reference to disease, interests that are only just now adequately before the public. With the opening of this library in his honor, I hope that an interest in the history of medicine will be strengthened and that the medical students will care to know of the work of those who have built up the medical profession in this community.

The memory of Henry Sewall is still so vivid with us that it will be almost as if we were speaking to him, but before we follow his work, it is fitting that we should pay tribute to two women who have contributed so generously to the life of this community. This library is not the only gift of Mrs. Denison to Denver. In the Fairmont School on West Third Avenue in this city is a children's library, the most charming I have ever seen. Its walls are covered with Copley prints of Abbey's paintings of the King Arthur legends and its shelves are well filled in the hope that many of the children may come to share one of Mrs. Denison's priceless possessions—a love of books. This is a memorial to her beloved granddaughter, Edith Swan. With rare vision Mrs. Denison has understood the value of research in the development of the medicine of our time. It was in memory of the ambition of her son to devote his life to medical research that she built a laboratory for this medical school while it was still in Boulder. It was in his honor that she has established the Henry Strong Denison Medical Foundation. This foundation has been active for thirteen years, seeking in the medical schools all over the country to find and to aid the group of young medical students who are especially gifted for research. Henry Denison was a student of mine, both in his early high-school years, when he showed himself to be a born naturalist, and later in the medical school, when his brilliant mind awoke to the joy of medical research. It has thus been one of the deepest gratifications of my life that Mrs. Denison asked me to share with his sisters, Mrs. Henry Swan and Mrs. John Jameson, the pleasure of finding the students for these awards. The awards have been given to students recommended by their teachers as those who should become the investigators and the teachers of the next generation. Indeed, many of our fellows are already on the faculties of medical schools. At the request of Mrs. Denison I have the honor to present to the Charles Denison Memorial Library these four bound volumes of the research of the students done under grants from this foundation. They are, of course, incomplete, for the work of these students goes on.

This medical school is also deeply indebted to Mrs. Henry Sewall. It was her loving care that made it possible for Dr. Sewall to devote his frail body and his powerful mind to the work that made him one of the great medical men of our time. This school wins great distinction because he taught here. As the city of Denver found out during the world war, Mrs. Sewall has rare gifts in organization that could have brought her recognition in her own right, but she chose rather to devote her abilities to help his work and she has thereby made herself beloved by all his medical friends throughout the country. Now she has given to the students in this medical school a lectureship, that succeeding classes of medical students may find inspiration and example in the life of Henry Sewall.

Last winter, starting to read all Henry Sewall's work, my eye lingered on the title page of the journal to which he sent his first article, Volume 1 of the *Journal of Physiology*, which was started in London in 1878. You too will be interested in this title page, for it reads:

> The Journal of Physiology
> Edited by Michael Foster, M.D., F.R.S.
> Professor of Physiology in the University of Cambridge
> With the cooperation in England of
> Prof. A. Gamgee, F.R.S., of Manchester; Prof. W. Rutherford, F.R.S., of Edinburgh; Prof. J. Burton-Sanderson, F.R.S., of Oxford
> and in America of
> Prof. H. P. Bowditch, of Boston; Prof. H. Newell Martin, of Baltimore; Prof. H. C. Wood, of Philadelphia.

Thus, when Dr. Sewall started his work in physiology in the laboratory of Newell Martin (1876–1881),

[2] A. M. Holmes, *Med. Rec.*, 50: 325, 1896.

England and America united to see if the English-speaking nations of the world might have enough research to fill one journal on the newer scientific medicine; not perhaps a whole volume every year, for the second volume spanned two years and the next one, three, but still enough to make a creditable journal. What a development Henry Sewall saw in his life-time! America was not without medical journals at that time. Indeed, there were thirty-five of them in all—sixty-four if the Canadian journals were included as well, some with quaint names, like the very first one, the *Medical Repository,* started a century earlier, 1797, or the *American Medical and Philosophical Register,* the *New-England Journal of Medicine and Surgery, and the Collateral Branches of Science,* or the *Medical Recorder of Original Papers and Intelligence in Medicine and Surgery,* but there was no journal at all to record the starting of the new era of the medical sciences initiated in the last decades of the nineteenth century. America, however, was not slow in transplanting the new European medical culture, as is made delightfully clear in Sewall's address on "The Beginnings of Physiological Research in America," published in 1923, in which he traces the lineage of Sharpey, Huxley, Michael Foster, Newell Martin, and we add Sewall.

Henry Sewall's first work was on the gastric glands, published a year before he received his degree, and I shall quote the first sentence in full. Mrs. Sewall will recall that one afternoon in early July, 1935, sitting in her lovely garden, we had both enjoyed Dr. Sewall's latest enthusiasm, namely, the discovery that all of us scientists write badly and that we all need to learn the art from the modern, the very most modern journalistic style. The memory of that delightful talk was with me as I turned his first page, and how glad I was that he had not made that last discovery too early but had rather inherited the gift of his father, who was called the "Silver-tongued Sewall," as well as the gift of his grandfather, who was a medical experimenter. These were Sewall's first words: "A prolonged investigation made on the stomachs of adult animals having failed in its object of giving me some insight into the functions of the different cells in the glands of the stomach, I determined to take up the question in another way; and by carefully examining the stomachs of embryos to seek if there was any correlation between the differentiation of certain cells in the embryo stomach and the first appearance of functional activity. This method, the results of which are here detailed, has not done all that I expected from it, but has nevertheless, I venture to hope, not been entirely fruitless." Then he proceeded to show that the power to split protein and to curdle milk was correlated with the appearance of the so-called chief cells, sound physiology of the present day. Sewall's first sentence really foretells the story of his life. The morning he died, he was still "seeking to gain some insight" into the processes of nature;—that phrase writes his autobiography and on that last day his experiments had not yet done all that he had hoped from them, but he was still in the joy of the making of new plans for his next steps.

To return to the young student of medicine. After winning the doctor's degree in Baltimore he went to Europe and worked with Kühne in Heidelberg, with the great physiologist, Ludwig, in Leipzig, and with Michael Foster at Cambridge. Kühne had only just made the brilliant discovery of the visual purple which developed in the retina during the intervals of darkness. With him Sewall published two papers on this remarkable pigment; this work laid the foundation for his interest in the physiology of the special senses, to which he returned again and again in studies on the eye and on the sense of equilibrium.

When an instructor in Baltimore, for he assisted Newell Martin from 1876 to 1881, while getting his degree (1879), Sewall worked not only on the physiology of gastric secretion but also on muscle-nerve preparations, the universal introduction to physiology at that time. He found that a stimulus not of itself strong enough to cause a reaction nevertheless modifies the reaction to succeeding stimuli. This is a part of every course in physiology to-day. In Ludwig's laboratory he continued to work on this subject with Professor von Kries, and in Cambridge he worked on the evidences of function in the cells of the gastric glands with Professor J. N. Langley.

Returning from Europe after two years, Sewall was appointed professor of physiology at the University of Michigan (1882–1889). In the brief time he was there, but eight years, Sewall made two major discoveries in physiology, work of such significance that, according to Dr. William H. Howell, it placed him in the front rank of physiologists. The first of these discoveries was on the sensory mechanism of the heart. Trained by Newell Martin and then by Ludwig, it was natural that Sewall should turn his attention to the heart. What a description Sewall has given of Martin's discovery of the method of isolating the mammalian heart! He wrote, "I very well remember one morning, I think that it was in the fall of 1880, Martin said to me in effect, 'I could not sleep last night and the thought came to me that the problem of isolating the mammalian heart might be solved by getting a return circulation through the coronary vessels.'" Later, of course, Sewall saw Martin carry the experiment through (SCIENCE, 1923).

Starting at Michigan, Sewall worked on the action of the nerves of the heart, and in an article on the

depressor nerve, published with his assistant, D. W. Steiner, he showed that the heart has to be considered not only as a motor mechanism but "as a sensory organ which might appreciate changes of pressure and in turn set into action a reflex apparatus" through the brain to be returned as motor impulses to the heart muscle. Dr. Howell has told me that this work foreshadows in everything but name and the precise location of the sensory endings the discovery of the sensory functions of the carotid sinus and the arch of the aorta. This work, while known to physiologists, has not yet been sufficiently realized by the medical profession as a whole.

Sewall's second beautiful discovery was acclaimed in the recent award of the Kober Medal (1931). In 1887 Sewall published an article in the *Journal of Physiology,* entitled "Experiments on the preventive inoculation of rattlesnake venom," in which, for the first time, he described the immunization of an animal to a foreign protein. The tablet erected at Ann Arbor in honor of this discovery reads as follows:

Commemorating
The pioneer work of Henry Sewall
Professor of Physiology
At the University of Michigan
from 1882 to 1889.
His work in immunizing animals against snake venom
demonstrated the principle
of antitoxin production.

This demonstration by Dr. Sewall anticipated by a half dozen years the discovery of antitoxic immunity by Behring and Ehrlich. The year that Sewall announced this work, 1887, was the year of his marriage to Miss Isabel J. Vickers, of Toronto, Canada, and one can not but wonder how clearly either of them realized what undying fame this work was to bring to Sewall. We shall now be able to show that these two major discoveries of Sewall's have run like a silver thread through all the research of his mature years.

Shortly afterward the symptoms of tuberculosis, which had developed as early as 1885, made Dr. Sewall resign his professorship at Michigan (1889) and go to Saranac with Trudeau. One misses, however, a record of any such period of rest as Dr. Sewall would later have imposed upon his own patients, for he at once became resident physician at the Cottage Sanatorium and there was apparently no interruption to his research. While at Saranac, Sewall started to work with the tubercle bacillus on a problem which was suggested to him by the late William Henry Welch of Baltimore. It was to compare the form and the staining characteristics of tubercle bacilli from the sputum of rapidly advancing cases with those from more quiescent cases, and in turn to compare these findings with bacilli from cultures known to be highly virulent and attenuated. He found that the organisms from advancing cases, like those from highly virulent cultures, were short rods, staining uniformly, while from the regressing cases the bacilli were long and markedly beaded. This has been fully confirmed and is in agreement with the most advanced bacteriology of to-day. Have you noticed that the words, exactly as they are known to-day, occur again and again like a refrain in regard to Sewall's work?

After a brief stay at Saranac, indeed less than a year, the Sewalls came to Denver. Here Dr. Sewall became professor of physiology in this medical school, the Denver and Gross, as it was then called, and started in the practice of medicine. In that day training for the pratice of medicine, as far as it was based on the underlying medical sciences, reflected pathology. This was true of the training of the elder Janeway in New York and of Osler in Baltimore. Sewall came into clinical medicine, as it were, by accident, and through physiology, and he therefore represented a type of clinician only just now coming to the fore through the newer discoveries centering around physiology and biological chemistry. Thus he was ahead of his time and it is exceedingly interesting to follow the clinical work of this physiologist turned physician. He published in all twenty-one articles on the heart and blood vessels, together with six more on special diagnostic methods for heart and lungs. While still at Ann Arbor he made a study with Myra E. Pollard on breathing, in which he recorded carefully the accurately toned voice sounds heard through auscultation of the lungs. Miss Pollard was a singer, and from this article I should judge that Sewall had a musician's ear far beyond the average, sensitive not only to pitch but to fine gradations in the qualities of sound, a gift without which no one can ever become highly expert in those methods of diagnosis that depend on the sense of hearing. Evidence of this highly skilled differentiation of qualities of sound occurs again and again in his clinical papers, as, for example, in the article on analysis of voice changes in the auscultation of the lung for the diagnosis of early lesions in the lungs.

Directly stemming from his early studies on the heart is his work on the action of the papillary muscles as well as analyses of the action of the cardiac valves taken from observations on his patients. For example, he found evidences of slight leakages of the atrioventricular valves occurring so frequently and transiently that he concluded they are to be considered as a safety device for an over-distended ventricle, and thus as a physiological mechanism. Another illustration is his use of the variations in blood pressures with varying postures to evaluate the state of a patient.

In 1921 Sewall published a paper with Dr. Samuel Swezey on the effects of limiting respiratory movements of the chest in certain cases which had then been found refractory to pneumothorax. In discussing the technique of so restricting the chest, he referred to the work of Dr. Denison in these words: "In fact, a Colorado medical pioneer, the late Charles Denison, probably left little to be accomplished in this regard beyond his ingenious devices for unilateral immobilization of the chest." The success of pneumothorax and the development of chest surgery have supplanted this work of Dr. Denison, but no one can read his papers on the subject without admiring his really great skill. From the historical aspect it is interesting to record that when Denison first described his method of immobilizing the chest, before the twenty-ninth annual convention of the Colorado State Medical Society, in 1899, he referred to the demonstration of Forlanini's method of pneumothorax which had been made here in Denver by the surgeon, J. B. Murphy of Chicago, just the year before.

As the years went on, Sewall's mind became occupied more and more with the subject of tuberculosis, and here his research was based on his own discovery of the immunizing properties of foreign protein. His early experiments had been made with snake venom; now he turned to other proteins, especially tuberculoprotein, as sensitizing agents. With his friend, the surgeon Cuthbert Powell, Sewall carried on an extensive series of experiments on the sensitization to foreign protein, using the nasal route of instillation. In the last article in this series, published in 1925, Sewall wrote as follows: "Some twelve years ago I became impressed with the idea that the surface epithelium of the body, including the epidermis and the succulent coverings of the respiratory and alimentary canals, must have most important functions in mediating between foreign material brought in contact with it and the internal tissues which it covers. From either a physiological or pathological point of view, the surface epithelium forms the "first line of defense" of the body. Our modicum of knowledge respecting the protective attributes of this covering embraces two certainties—that it is a mechanical barrier intervened to the passage of foreign material, especially when particulate; and that, when part of a mucous membrane, it is a mobilizing organ, capable of chemically changing foreign substances in contact with it." Here I can not but digress for a moment to recall that Sewall's grandfather, who was graduated in medicine from Harvard in 1812, was the first to demonstrate absorption through the skin by immersing a part in a solution of madder and finding excretion of the dye through the kidney. Returning to the experiments of Sewall and Powell, they dropped minute doses of horse serum into the nose of guinea pigs, repeating this procedure daily first on one side and then on the other, and after an appropriate interval tested the animals with an intravenous injection of the same serum. Most of the animals died with typical anaphylactic shock, showing that they had been sensitized to the foreign protein; but a few survived, and of these they wrote that they might have considered them as mere failures of absorption of the serum had they not found that they did not react to a second intravenous injection of serum twenty-four days after the first. They concluded that the original injections had immunized instead of sensitized. With carefully graded doses they found that larger doses tended to sensitize, smaller to immunize. In these experiments some of the sensitized guinea pigs showed, on re-injection, bronchial spasms simulating asthma. Sewall concluded that in the case of the human disease, certain individuals had been subjected early to foreign protein in amounts sufficiently large to sensitize rather than to the smaller doses which might have immunized.

Sewall also made extensive experiments on the effects of re-breathed air on normal and tuberculous guinea pigs, putting them in jars, six in series. He obtained some evidence of a slight sensitization to a foreign protein. These results are at variance with the prevailing views, namely, that the ill-effects experienced in close rooms are due merely to moisture and to the still air. Sewall's experiments, on the other hand, show that tuberculous guinea pigs died sooner and with more extensive lesions after prolonged exposure to re-breathed air.

The thought of sensitization runs through all these experiments and finally led Sewall to a re-study of the Koch phenomenon. For fifty years this has been a crucial problem in tuberculosis, and thus for the benefit of the non-medical part of my audience I must define this phenomenon. Koch described the effects of a first injection of tubercle bacilli into the subcutaneous tissue of a guinea pig, saying that at first there was little or no reaction that could be seen or felt, but that after about two weeks there developed a hard nodule which increased in size slowly, then ulcerated through the skin and formed a draining sinus which never healed. Quite different, on the other hand, was the progression of events after a second inoculation; on the next day there was a marked reaction, with swelling, redness and induration; these signs then regressed and again a hard nodule developed which either did not break down or, if an ulcer formed, it healed promptly. These events of re-inoculation are called the Koch phenomenon and they show that a primary infection changes the reactions of the body toward the re-introduction of tubercle bacilli. In this phenomenon is bound up the question of increased

resistance or acquired immunity to this disease, and thus the solution of the problem of the mechanisms involved has remained a major question in tuberculosis.

In 1934 Sewall, with two of his students, de Savitsch and Butler, made an important study of the time relationships between the two inoculations and found that there was an optimum period for the second inoculation, as shown by a decrease and a fibrosis in the lesions of the first infection. The lesions of the primary inoculations were visceral, it having been repeatedly demonstrated by many observers that there is a restriction of the invasion of the bacilli of the second injection. If the re-infection followed too soon, as in two or three weeks, Sewall found that the visceral lesions were enhanced, but between the fiftieth and ninetieth days the effects of re-inoculation were the most favorable.

At the time of his death Dr. Sewall, still working on this problem, was studying the effect of a re-inoculation done by the intradermal route in two different places at the same time, one near the site of the primary injection and the other on the opposite side of the body, far from the original point. He was led to plan this experiment in the hope that it might throw some light on the clinical finding that during periods of regressing lesions in one lung, lesions that advance may spring up in the other. In this study, Sewall, working with the last medical student who had the privilege of assisting him, namely, Gerald J. Duffner, had made exceedingly careful discriminations between the true nodule or tubercle in the dermal or subcutaneous tissues and the inflammatory reactions around the tubercles. They found that the true nodule or tubercle which formed near the primary lesion was smaller than the one on the opposite side and postulated that the processes to be summed up as immunity might be greater near lesions than at a distance from them.

Mrs. Sewall has entrusted me with the pleasant task of finishing these experiments, and I must now give a partial report of the work. In the introduction to the paper on this work which Dr. Sewall had started to write, are these words, "The question whether allergy favors, opposes, or has nothing to do with the development of specific immunity in tuberculosis still invites experimental observation." That states the problem. Then he continued, "When a guinea pig is inoculated with a virulent strain of human bacilli and examined post mortem after three or four months, there is a lack of quantitative relationship between the effects of a large range of doses and the extent of lesions produced. The pathologic lesions may fail to differentiate strongly between two infections of which one is one thousand times as great by weight of milligrams as the other." Here he states one of the difficulties which has been a block in all the experimental studies which have sought to evaluate measures which might increase or decrease resistance to tuberculosis, that is, the tremendous variations in the effects of a given dose of bacilli, no matter how carefully and accurately measured. Our results, which are like those of others, have given a spread in survival time from fifteen to 738 days in rabbits inoculated with the same weight of bacilli, bovine strain B-1; while in guinea pigs inoculated with the human strain H-37 the survival time has varied almost as widely. This difficulty has now been overcome by a young man in my department, Dr. Kenneth C. Smithburn. He has been able to reduce the spread in death rate of guinea pigs inoculated by the intracerebral route to a minimum. How I should love to have told these results to Dr. Sewall! They depend on the newer phase of bacteriology known as dissociation. That bacteria grow in two different forms was discovered in 1921 by Arkwright and independently by de Kruif and Northrop the same year. Petroff was the first to apply this discovery to the study of tubercle bacilli and, with his assistant at Saranac, dissociated the avian strain into rough and smooth forms and determined that they were of widely different virulence. They also made what now proves to have been a partial dissociation of bovine and human forms. Dr. Smithburn, using an exact adjustment of the hydrogen ion concentration of the culture media, made possible by a modification of the glass electrode by Dr. D. A. MacInnes at The Rockefeller Institute, found that tubercle bacilli are highly sensitive to acids and alkalis. For his purpose he found Dr. Corper's glycerol-egg-yolk medium the best, and by adjusting this medium to different pH values he obtained three different types of colonies from freshly isolated human and bovine strains. They are, first, smooth, glistening colonies that look like moth balls; second, the markedly corrugated colonies in which the bacteria climb over one another from the surface of the media in patterns long held typical of the growth of acid-fast organisms, and third, flat, spreading colonies. The flat, spreading colonies, and indeed the smooth ones, were seen as far back as 1909 with the acid-fast organisms that infect the cold-blooded animals, but their meaning was not then understood. Dr. Smithburn has shown that the bacilli of the smooth colonies are highly virulent, of the rough colonies attenuated, and then concerning the organisms of the flat colonies he has made the significant discovery that they are not composed of organisms intermediate in virulence but of mixtures of virulent and attenuated forms in different proportions. By analyzing our records of survival time and type of disease in rabbits inoculated with the undissociated

tubercle bacilli, Dr. R. M. Thomas had found that the animals could be separated into three groups; one group that died within the first 100 days with an acute infection; an intermediate group that died during the next 100 days, and a third small group that survived about a year and showed chronic lesions. With Dr. Smithburn's dissociated organisms it is possible to separate these three groups at will. With the old undissociated strains it is as if one were drawing out of a bag handfuls of tiny balls, part white and part black; one might get a handful predominately black, or predominately white, or approximately about equally mixed, but the chances of drawing twice exactly alike would be extremely slight. Thus, with the old cultures, one could never have any two animals with the same dose of the kind of bacilli that really count, namely, the virulent ones. But with the dissociated strains, all the animals that receive the virulent organisms die in the acute phase; all with the attenuated survive into the later period, while those with the organisms from the flat colonies die in the intermediate phase with some tendency to overlap into the acute phase. Thus one difficulty in experimental tuberculosis has been eliminated. Under the old conditions we had postulated marked differences in the resistance of the animals; now we know this assumption to have been only partly correct because we did not take into account the haphazard selection of the virulent organisms in the dosage. These newer strains are probably not wholly pure, for there has been no selection of colonies, but they are sufficiently pure to enable one to detect real, if slight, differences in resistance because the spread of the death rate is proportional to the reduction of the dose. Thus this new knowledge eliminates one variable.

To return to Sewall's last work, his experiment has now been repeated by Dr. A. L. Joyner, in my department, and myself. We have confirmed the observation of smaller nodules on the side near the primary lesion which we call the "Sewall Phenomenon," but we have not yet been able to carry the work to a convincing conclusion. Sewall's descriptions of the reactions, as made out by feeling the nodules, were so clear that they were readily followed. We used the intradermal route, the dosage and time intervals recommended. The site of the primary inoculation, as is conventional, was in the right inguinal region; the distant secondary one was on the left side with its nearest drainage toward the axilla. When the primary nodule developed after the first inoculation, we removed it from one animal. It had developed in fourteen days; the wound healed promptly and never ulcerated. The nodule was made of two small intradermal tubercles, each of which contained in one section fifty to sixty tubercle bacilli. This number of bacilli in so small an area represents high virulence. The culture we used was the human strain H-37, which had been grown by Dr. Smithburn at pH 6.8 for eight generations. The secondary inoculations were made with reduced dose in ninety days.

We have plotted the curves of our reactions: There were immediate redness, swelling and induration, typical of the Koch phenomenon, somewhat larger on the left side than on the right. It was like a tuberculin test and faded at the same rate; it was practically gone in four to five days. Later, in about fourteen days, the true nodules, or tubercles, started and increased in size at about the same rate as had the nodules of the primary inoculations. Unlike the primary nodules, they never ulcerated. At the end of one month these nodules averaged a little larger on the left side than on the right. All these observations are in confirmation of those of Sewall and Duffner. They may indicate that there is slightly more resistance near the first inoculation, as Sewall postulated, but I must now tell you of the complications of our experiment. We sacrificed the animals at different intervals, but those that lived beyond a month began to show new accessory nodules around the primary inoculation. They were all true tubercles, as proved by sections of them, and ultimately they made the amount of tuberculous tissue on the right side far exceed that on the left. This is the phenomenon that makes the problem so complex.

We then began to study the two areas of skin, which Sewall had made so interesting to us, by means of injections of a soluble dye which was being used by Dr. Philip McMaster at the Rockefeller Institute for the study of lymphatic drainage. Dr. McMaster has found a dye, pontamine sky blue, so innocuous that he could use it in his own arm, for it caused no reaction and ultimately faded completely. We found, as had he, that every intradermal injection of this dye reveals lymphatics instantly. This is because the plexus of lymphatic capillaries of the dermis is so abundant that one can not introduce a needle to that level without puncturing them. This means that dye is injected into dermal lymphatics under such pressure that it drains quickly into the deeper subcutaneous plexus and spreads a considerable distance. When the needle enters the subcutaneous level, on the other hand, the lymphatics may or may not be punctured, and often the dye enters them by the slower physiological route through their walls. These experiments with the dye showed us that our intradermal injections of bacilli had forced some of them into lymphatics under pressure so that they had been quite widely dispersed at the moment of the injection. Thus the nodules that develop in the dermis at the point of the

injection can not tell the whole story, and one must know what becomes of the bacilli rather widely scattered in the subcutaneous tissues. The reason that so many more of the accessory, late nodules develop on the right side lies in the fact that the right inguinal nodes, always massively caseous from the primary right inguinal inoculation, offer more of a block to the drainage of the bacilli of the second inoculation than the normal or more nearly normal left axillary nodes.

Numerous studies of the Koch phenomenon, made during the fifty years and more since Koch first described it, have shown that in the previously infected animal there is not only restricted dissemination of reinjected tubercle bacilli, but reduction in their numbers and some change in their form. This has been found by Rist and Rolland, Kraus, Willis and many others. We have counted the bacilli in the sections of all the secondary tubercles, both the early ones and the later, and have found but few bacilli, one or two, up to five, in tuberculous lesions many times as large as the original primary tubercle that contained fifty or sixty bacilli. Moreover, many of these bacilli have been long and beaded, as Sewall had described the organisms of healing lesions and attenuated cultures years ago. With the development of the multiple late lesions, there were ultimately many more residual bacilli on the right side than on the left, for every tubercle has shown at least one bacillus. The nodules were at varying distances from the primary lesion, but they complicate the experiment and we must devise a plan which will obviate this difficulty. The fate of the bacilli, either their death or their attenuation, seems to us the crux of the Koch phenomenon or the immune reaction.

Recent studies on the reactions of the body to acid-fast organisms have stressed the factors which are common to all these organisms. Tuberculous lesions form after the injection of acid-fast organisms whether the bacilli are virulent or avirulent, as well as whether the bacilli are living or dead. Lesions from living, virulent bacilli progress in animals that are susceptible to the strain. Lesions from attenuated, avirulent or dead bacilli regress. Similar lesions can also be produced by lipoids extracted from all types of tubercle bacilli, virulent or avirulent, or from bacillary residues. The tuberculo-proteins have also been shown to have much in common. An example of this is to be found in the fact that the tuberculin prepared by the government for the testing of cattle is made not from bovine strains with which the cattle are infected, but rather from three virulent human strains. It is probable that human strains were selected because they are less apt to show loss of virulence under cultivation than are bovine strains. When we come to know the materials that differentiate the strains from one another and the virulent from the avirulent forms, it may be possible to probe deeper into the mechanism by which the more virulent strains survive in the infection. We already know that even susceptible animals have some power to degrade the virulence of tubercle bacilli. The mechanism of this degradation of virulence is the enigma of the Koch phenomenon.

In the last manuscript of Dr. Sewall is another sentence which I wish to quote; it refers to this long, difficult and unfinished task of solving the Koch phenomenon. He wrote: "It seems important that discrete facts spontaneously occurring or artificially established continue to be assiduously collected and arranged in a way to establish the inevitable sequence and hence a meaning." How true these words, and how well they express the adventure which is research to which he devoted his energies with joy to the very last day of his life!

OBITUARY

SIGMUND GRAENICHER

DR. GRAENICHER died on September 16, having been in poor health for some years. He was a naturalist in the broad sense, especially interested in entomology. He was born at Natchez, Mississippi, on April 29, 1855, of Swiss parents. His mother and father died within a week of each other of yellow fever, when he was only three months old. In his early childhood he was in the loving care of an old Irish couple, but when twelve years old he was sent to Switzerland to be educated. His uncle, to whom he was consigned, wished him to be an engineer, and accordingly he attended engineering courses at Stuttgart and in the Polytechnikum at Zurich. On the death of his uncle, Graenicher felt free to give up the engineering, for which he had little inclination, and to devote himself to biological subjects. He studied marine life at Nice, and obtained his Ph.D. at Basel in 1884. Expecting to return to the United States, he entered the field of medicine and after working for a time at Bern, he took his degree "Summa cum Laude" at Munich in 1888. He had in the meanwhile been married, and the couple came to Milwaukee, where Graenicher took up the practice of medicine. Very soon, he became associated with the Museum of Natural History at Milwaukee, which in those days was especially known from the brilliant work of Dr. and Mrs. Peckham on spiders and wasps. Graenicher began by building up the collection of fishes, which he found to consist of only two specimens. For years he worked as honorary

curator, and was also active in the work of the Wisconsin Natural History Society. In 1909 he gave up the practice of medicine and became curator of invertebrate zoology at the museum. In this position he actually covered the whole field of biology, and when he left it was necessary to find a zoologist and a botanist to continue his work. In 1916 he retired from the museum and moved to Florida, largely on account of his health. He established himself at South Miami, making a home out of a veritable wilderness, and in so doing probably overtaxing his strength, so that he was a semi-invalid from about 1926. In 1925 he was able to visit Switzerland.

It is difficult to estimate the value and influence of such a man, but it was great and still continues. Essentially an out-of-door naturalist interested in the relations and interactions of all forms of life, seeing life as a whole, he was of a type now too rare. His zeal knew no bounds, and what he did was only limited by his time and strength. He began to publish in 1903 and 1904 on the bees of the large genus *Andrena*. These had been intensively studied by Robertson at Carlinville, Illinois, but Graenicher found that in his more northern locality many of the species were different and new to science. The study of these and other bees included investigations of their life-histories, their parasites and their relation to the flowers visited. Many discoveries were made, and our knowledge of the structure of bee larvae and of the parasitic habits of several native bees is derived from Graenicher's writings. The work on bees and flowers led naturally to consideration of other flower visitors, and thus special attention was given to certain families of Diptera. Certain flower-loving beetles (*Nemognatha*) were also investigated. In 1935 appeared an elaborate paper on the bee fauna and vegetation of Wisconsin, and in 1930 a similar paper gave the results of his work in the Miami region of Florida. I have a list of 25 papers published by Graenicher, nine of them issued by the Wisconsin Natural History Society.

There have not been many workers in this country who have studied the flower-visiting insects intensively in a particular locality. We think of Graenicher in Wisconsin, Robertson in Illinois, Lovell in Maine. This kind of work offers rich rewards in the way of discoveries, in any part of the country, and would doubtless be more popular if better understood. It is advanced "nature study," of broad cultural value, but demanding much time and labor. It should be especially valuable to those who teach biology in our high schools. It must be promoted by men of the Graenicher type, who combine enthusiasm with knowledge and are not afraid of a fact because it is not mentioned in the books. Unfortunately, no really adequate book on the subject is available at the present time. The existing records furnish a basis for such a book, but it is very difficult for any beginner to assemble or find the papers in which they are printed. Is there not some publisher who will produce for us a work of the same general character as Rayment's "Cluster of Bees," lately issued in Australia? The necessary author or authors could probably be found, and perhaps the work might be ready in a few years. A similar work on ants, as a memorial to Wheeler, has been suggested.

Graenicher's body was cremated; he wished that there should be no regular services at the time of his funeral, but hoped that his friends might assemble one day on a pleasant afternoon under the trees and speak kindly of him. These friends are widely scattered, but perhaps the above account may serve to stimulate such conversation in many places. For the main facts concerning Dr. Graenicher's life I am indebted to his daughter, Mrs. Sylva G. Martin.

T. D. A. COCKERELL

UNIVERSITY OF COLORADO

RECENT DEATHS AND MEMORIALS

LORD RUTHERFORD, director of the Cavendish Laboratory of the University of Cambridge, died on October 19, at the age of sixty-six years.

DR. FRANK MORLEY, since 1900 until his retirement as professor emeritus in 1929 professor of mathematics at the Johns Hopkins University, died on October 17 at the age of seventy-seven years.

SAMUEL HUME BECKETT, professor of irrigation investigations and practice at the University of California, died on September 17 at the age of fifty-four years.

DR. JOHN NAPOLEON BRINTON HEWITT, linguist and ethnologist of the Bureau of American Ethnology, Smithsonian Institution, died on October 14. He was seventy-seven years old.

HENRY KENDALL MULFORD, president of the Mulford Colloidal Laboratory, Philadelphia, and director of the research and biological laboratories of the National Drug Company, died on October 15 at the age of seventy-one years.

SENATOR ALESSANDRO LUSTIG, formerly professor of general pathology in the University of Florence, known for his work on bubonic plague and sanitation, died on September 23. He was seventy-nine years old.

DR. MAX HOLLRUNG, professor of plant pathology at Halle, died on May 5 in his seventy-ninth year.

FRANK STEPHENS, pioneer west coast biologist, first

director of the San Diego Natural History Museum, and widely known field naturalist, died in San Diego on October 5, as the result of a street-car accident on September 25. He was in his eighty-ninth year, having been born in Livingston County, New York State, on April 2, 1849. Driving a yoke of oxen, he first arrived in California in 1876. Thereafter he lived most of the time in southern California, and since 1897 made his permanent home in San Diego. A fellow of the American Association for the Advancement of Science, fellow of the San Diego Society of Natural History, member of the American Ornithologists' Union, the American Society of Mammalogists, the Cooper Ornithological Club and other scientific organizations, he was originally known as an ornithologist, although he later became remarkably versatile in his interests. Among his publications are "Life Areas of California" (1905); "California Mammals" (1906); "An Annotated List of the Birds of San Diego County, California" (1919); "An Annotated List of the Mammals of San Diego County, California" (1921); "An Annotated List of the Amphibians and Reptiles of San Diego County, California" (1921); "Notes on the Marine Pleistocene Deposits of San Diego County, California" (1929). In 1910 he donated to the San Diego Society of Natural History his private collection of some 2,000 birds and mammals, thereby laying the foundation of its subsequent continuous activity in these departments. He is survived by his widow, Mrs. Kate Stephens, who has been his close collaborator and companion in his scientific work.

C. G. A.

AT the Founders' Day exercises of Lehigh University on October 6, honor was paid to the memory of the late Dr. Henry S. Drinker, '71, president of the university from 1905 until 1921, and to the late Dr. Natt M. Emery, formerly instructor, registrar, acting president, vice-president and controller during his forty years' service for the university. Eugene G. Grace, '99, president of the board, spoke in honor of Dr. Drinker, and a 16-foot oak tree was planted on the campus. In memory of Dr. Emery, a bronze tablet, recently placed in Packer Memorial Chapel, was unveiled. The speaker was Dean Philip M. Palmer.

Nature states that in commemoration of the birth of J. D. v. d. Waals on November 23, 1837, an international conference on interaction between molecules will be organized by the "van der Waals Fonds" and the "Nederlandsche Natuurkundige Vereeniging." The ordinary sessions will be held in the van der Waals laboratory in Amsterdam on November 25 and 26, and an official celebration will take place on November 27. The object of the conference is to give a survey of some of the recent work connected with the idea of van der Waals forces. The program will be published later. Sufficient time will be left for general discussion. A special number of *Physica* will appear during the conference; it is hoped to be able to publish in this issue a number of papers on a variety of questions having some relation to the work of van der Waals. Members of the organizing committee are Professor J. D. v. d. Waals, Dr. A. Michels, Professor J. A. Prins and Dr. H. B. G. Casimir.

SCIENTIFIC EVENTS

CAMPAIGNS FOR FUNDS TO FINANCE MUSEUMS

The Museum News states that plans calling for the raising of large additional funds have been adopted by the American Museum of Natural History, the Pennsylvania Museum of Art and the University of Pennsylvania Museum.

The American Museum is proposing to raise ten million dollars for a ten-year development program in all departments and to provide increased annual income of $431,000. The plan includes an increase in the museum staff, salary adjustments, completion of present exhibit programs and development of new exhibit halls, and expansion of the educational work. A committee to direct the campaign includes F. Trubee Davison, general chairman; A. Perry Osborn, executive chairman; Mrs. Winthrop W. Aldrich, vice-chairman, and E. Roland Harriman, treasurer.

The Pennsylvania Museum of Art has announced a ten-year program which will involve the addition of $10,428,000 to the funds for the museum and $5,117,000 for the museum's textile and industrial schools. The funds for the museum would include $368,298 to complete payment for the Foulc Collection, $2,500,000 for completing the interior of the museum, and $7,560,000 for endowment for purchases, operation and education. The school funds would include $2,825,000 for a new building, $500,000 to pay off a mortgage and the remainder for endowment.

The University of Pennsylvania Museum has announced a plan for raising a fund of $500,000 in connection with the university's bicentennial celebration. Out of this fund $287,000 is needed to carry on research programs in the field—in the Near and Far East, the Iranian Valley, the Indus Valley, the Mediterranean area and North and South America. The remainder would be used for the museum's educational program, including a publication fund.

COLLECTIONS OF MEXICAN FOSSILS AT THE UNIVERSITY OF MICHIGAN

THE Museum of Paleontology of the University of Michigan has been the recipient of a valuable collection of slides of fossil foraminifera prepared and presented by Mr. R. Wright Barker, paleontologist of the Compañia Mexicana de Petroleo "El Aguila," S. A., Tampico, Mexico. The collection contains 72 species, represented by several hundred specimens, from the Upper Cretaceous and Tertiary formations of the Tampico region, Mexico. For several years Mr. Barker has been engaged in studying the micro-faunas of the geologic formations in eastern Mexico, and recently he published a chart showing the stratigraphic range of 231 of the more characteristic foraminifera in the Tampico Embayment. The collection which he now presents to the University of Michigan contains the species on which the chart is in part based. It is the first installment of a complete set to be deposited at the university to assure the preservation of valuable material which might eventually become lost or unavailable to science. This unique gift has been accepted by the regents of the university and will be known as "The Barker Collection."

In July, 1936, Mr. John Muir, of Fort Worth, Texas, deposited his collection of core samples, well cuttings, outcrop samples and fossils from eastern Mexico in the Museum of Paleontology at Ann Arbor. This material was used by Mr. Muir in the preparation of his book, "Geology of the Tampico Region, Mexico," and is therefore, in a sense, considered as type material.

A large number of marine invertebrate fossils, collected in 1925 in northern Mexico by geologists of the East Coast Oil Company under the direction of Professor Charles Lawrence Baker, were turned over to the University of Michigan in 1928. They have been the basis for paleontological studies recently published by Dr. R. W. Imlay and supported by the Horace H. Rackham School of Graduate Studies.

Because of the intensive regional geologic studies which have been carried out in Mexico during the past eight years under the auspices of the university, and the large collections of fossils which the expeditions have brought to the Museum of Paleontology, this museum is regarded as a logical center and depository for research material on which stratigraphic and paleontologic studies of Mexico are based.

LEWIS B. KELLUM

EXPEDITIONS OF THE FIELD MUSEUM OF NATURAL HISTORY

A REPORT of the expeditionary work of the Field Museum of Natural History during 1937 has been made public by Dr. Clifford C. Gregg, director of the Museum.

The Archeological Expedition to the Southwest, under the leadership of Dr. Paul S. Martin, chief curator of anthropology, has been charting and excavating prehistoric Indian sites in southwestern Colorado, not far from Mesa Verde National Park. A large collection of artifacts has been obtained, and the research conducted has yielded information which throws new light on the little-known history of the early aboriginals of the region.

The Botanical Expedition to Southeastern Mexico, led by Llewelyn Williams, curator of economic botany, recently completed its work in the Isthmus of Tehuantepec and parts of the states of Oaxaca and Veracruz. About 600 specimens of woods, 8,000 herbarium specimens, a large amount of palm material and several hundred photographs were obtained.

Dr. Julian Steyermark, assistant curator of the herbarium, spent the summer in making a collection and study of the flora of Missouri.

Professor A. C. Noé, of the University of Chicago, research associate in paleobotany, spent the summer in a study of the flora of Panama, working at the Barro Colorado Island Biological Station in the Canal Zone.

J. Francis Macbride, associate curator of the herbarium, continued his work, begun in 1929, of making photographs of type specimens of plants in European herbaria.

Bryan Patterson, assistant curator of paleontology, led the Paleontological Expedition to Colorado, obtaining a collection of important fossil mammals. He was assisted by James H. Quinn. Elmer S. Riggs, curator of paleontology, joined the party for a few weeks.

An extensive collection of rock specimens, illustrating various phenomena relating to the structure of the earth, was obtained by Sharat K. Roy, curator of geology, on an expedition in mountainous regions of Colorado.

Dr. Wilfred H. Osgood, chief curator of zoology, spent several months in French Indo-China, during which he collected some 500 mammal, bird and reptile specimens, including material for several habitat groups.

A Zoological Expedition to South America, which left in January, under the leadership of Emmet R. Blake, assistant curator of birds, is still in the field. Material for a habitat group of the rare and unusually interesting bird known as hoactzin has been obtained, as well as a large general collection of birds, mammals, reptiles and other kinds of animals of British Guiana and Brazil.

C. J. Albrecht, staff taxidermist, conducted an ex-

pedition during the summer to the Pribilof Islands, near Alaska, where he collected fur seals for a proposed habitat group.

Alfred C. Weed, curator of fishes, accompanied by L. L. Pray, staff taxidermist, collected representative fishes of the Atlantic Coast on an expedition to Frenchman's Bay in Maine.

Karl P. Schmidt, curator of reptiles and amphibians, headed two field parties. On the first, to mountain and desert regions of Arizona and California, he was accompanied by Leon L. Walters, staff taxidermist, and Dr. Alfred E. Emerson, of the department of zoology of the University of Chicago. On the second, to western Texas, he was accompanied by D. Dwight Davis, assistant curator of vertebrate skeletons, and Tarleton Smith, of the United States National Park Service. Both expeditions obtained important herpetological collections.

LECTURES AT THE COLLEGE OF PHYSICIANS OF PHILADELPHIA

A SERIES of scientific lectures will be held on the first Wednesday of each month, beginning on October 6, at the College of Physicians of Philadelphia. The lecturers and their subjects are as follows:

James M. Anders Lectures: Dr. H. C. Sherman, Mitchill professor of chemistry, Columbia University: "Optimal Nutrition as a Scientific Concept and an Economic Problem"; Dr. C.-E. A. Winslow, Lauder professor of public health, Yale University School of Medicine: "Housing and Health"; and Dr. C. Macfie Campbell, professor of psychiatry, Harvard Medical School: "Emotional Factors in Health and Disease."

Mütter Lecture: Dr. Edward D. Churchill, John Homans professor of surgery, Harvard Medical School: "The Pathology and Surgery of Bronchiectasis."

Weir Mitchell Oration: Dr. Detlev W. Bronk, Johnson professor of biophysics and director of the Johnson Foundation, University of Pennsylvania: "Cellular Changes in Nerve Activity."

Mary Scott Newbold Lecture: Dr. Harry Goldblatt, associate professor of pathology and associate director of the Institute of Pathology of the School of Medicine of Western Reserve University: "Experimental Hypertension."

Nathan Lewis Hatfield Lectures: Dr. Warfield T. Longcope, professor of medicine, the Johns Hopkins University School of Medicine: "Pathogenesis and Treatment of Streptococcal Infection"; and Dr. Charles H. Best, professor of physiology, University of Toronto: "Recent Experimental Work on Liver Function."

Mary Scott Newbold Lecture: Dr. Russell M. Wilder, professor of medicine, Mayo Foundation, Mayo Clinic: "Addison's Disease."

LAKE PLACID MEETING OF THE OPTICAL SOCIETY OF AMERICA

THE twenty-second meeting of the Optical Society of America was held at Lake Placid, New York, from October 14 to 16. The sessions were devoted to papers contributed by members on various aspects of optical materials. Among the speakers were: Dr. E. D. Tillyer, American Optical Company; Dr. George W. Morey, Geophysical Laboratory; Dr. W. B. Rayton, the Bausch and Lomb Optical Company; Dr. A. N. Finn, the National Bureau of Standards; and Dr. Donald C. Stockbarger, the Massachusetts Institute of Technology.

A special feature of the program was a motion picture made on the South Pacific eclipse expedition last June. It was presented by Professor F. K. Richtmyer, of Cornell University, and Dr. I. C. Gardner, of the National Bureau of Standards.

The Frederic Ives Medal, awarded biennially for distinguished work in optics, was presented to Dr. Herbert E. Ives, physicist at the Bell Telephone Laboratories, New York. He is the son of the late Frederic Ives, in whose honor it was established and is distinguished for his many contributions in all the departments of optical science. He is best known for his work on flicker photometry, stereoscopic photography, photoelectric cells, the transmission of photographs by wire and, more recently, his work in television.

The medal was presented to Dr. Ives at the annual dinner by Dr. Arthur C. Hardy, professor of physics at the Massachusetts Institute of Technology and president of the society. Frederic Ives, for whom the medal is named, died last May. He was internationally known for his development of the half-tone screen process used by newspapers and magazines in printing illustrations. He also made important contributions in the field of color photography and developed special types of optical apparatus.

Officers of the society elected for the coming year are: *President,* Professor R. C. Gibbs, Cornell University; *Vice-president,* Dr. K. S. Gibson, the National Bureau of Standards; *Secretary,* Dr. L. B. Tuckerman, the National Bureau of Standards, and *Treasurer,* Henry F. Kurtz, the Bausch and Lomb Optical Company.

AWARD OF THE CHEMICAL INDUSTRY MEDAL TO PROFESSOR CRANE

THE Chemical Industry Medal for 1937 has been awarded to Professor E. J. Crane, of the Ohio State University, who since 1914 has been editor of the *Chemical Abstracts* of the American Chemical Society.

The medal, bestowed annually for a "valuable application of chemical research to industry," has been awarded to Professor Crane for his work in abstracting technical and scientific papers in all fields of chemical industry. More than 60,000 abstracts are prepared and published annually by the staff at the Ohio State University, working under his direction. About

a third of the abstracts cover chemical patents. Nearly 3,000 scientific, technical and trade periodicals published in thirty-one languages are systematically examined and made available through *Chemical Abstracts.* It is the agency through which American research workers and industrialists are enabled to maintain continuing contact with the progress of chemical science in other nations.

The official statement giving the basis for the award reads:

> Under Professor Crane's editorship, the completeness of this abstract service has been developed and safeguarded and the abstracts have been supplemented by unusually thorough annual and ten-year indexes. The third Decennial Index, now in course of publication, will, for example, contain over 2,000,000 entries and will require about 9,000 large pages of fine print.

Professor Crane's publications have been chiefly in the field of chemical literature. For twenty-three years he has been chairman of the Committee on Nomenclature, Spelling and Pronunciation of the American Chemical Society. He has been active in the work of the Committee of the International Union of Chemistry for the Reform of Inorganic Chemical Nomenclature. He is the author of numerous reports on nomenclature, including "The Pronunciation of Chemical Words," which is widely used in radio-broadcasting. He is co-author with Austin M. Patterson of "A Guide to the Literature of Chemistry" and is a member of the Executive Committee of the Division of Chemistry and Chemical Technology of the National Research Council.

Professor Crane was born in Columbus, Ohio, on February 14, 1889, and was graduated from the Ohio State University in 1911. He has been associated with *Chemical Abstracts* since his graduation. He holds membership in the American Chemical Society, Sigma Xi, Phi Beta Kappa, Phi Lambda Upsilon, Lambda Sigma, Alpha Tau Omega and the American Association for the Advancement of Science. He is interested in community development and for two years served as mayor of Upper Arlington, Ohio.

The medal, formerly called the Grasselli Medal, which was founded in 1920 as an "annual tribute to distinction in applied chemistry," will be presented at a meeting of the Society of Chemical Industry on November 5 at the Chemists' Club, New York City. The presentation will be made by Dr. A. E. Marshall, of New York. Dr. Austin M. Patterson, of Antioch College, will speak on the life and accomplishments of the medallist, who will deliver an address on "Words and Sentences in Science and Industry."

Previous recipients of the medal have been: Allen Rogers, W. H. Fulweiler, B. D. Saklatwalla, E. R. Berry, C. R. Downs, Harold J. Rose, Bradley Stoughton, Per K. Frolich, L. V. Redman, G. L. Clark, James G. Vail, Floyd J. Metzger, Edward R. Weidlein and Walter S. Landis.

SCIENTIFIC NOTES AND NEWS

DR. WILLIAM J. ROBBINS, since 1930 dean of the Graduate School of the University of Missouri, has been appointed director of the New York Botanical Garden and professor of botany at Columbia University.

DR. LUDVIG HEKTOEN, of Chicago, chairman of the National Research Council and of the research committee of the American Medical Association, has been appointed executive director of the National Advisory Cancer Council, which, jointly with the Public Health Service, will be responsible for the administration of the National Cancer Institute act.

AMONG those on whom the doctor's degree, *honoris causa,* was conferred at the recent celebration of the hundredth anniversary of the University of Athens, were Dr. George D. Birkhoff, professor of mathematics at Harvard University and president of the American Association for the Advancement of Science; Dr. Irving Fisher, professor of political economy at Yale University; Dr. Haven Emerson, professor of public health administration and director of the Institute of Public Health of the College of Physicians and Surgeons of Columbia University, and Dr. Edward L. Thorndike, director of the Institute of Educational Research of Teachers College, Columbia University.

AT the seventy-third annual convocation of the University of the State of New York, the honorary degree of doctor of science was conferred on Dr. John C. Merriam, president of the Carnegie Institution of Washington, and on Dr. Alexis Carrel, of the Rockefeller Institute for Medical Research, New York City. The ceremony was the closing event of the convocation, at which the hundredth anniversary of the establishment of the State Museum was observed.

DR. FLORENCE R. SABIN, member of the Rockefeller Institute for Medical Research, New York, on October 8 was awarded the honorary degree of doctor of science by Oberlin College, on the occasion of its centennial marking the beginning of college education for women and of coeducation.

ALUMNI membership in the Society of Sigma Xi has been conferred by the Cornell chapter on Dr. Edward Bausch, chairman of the board of the Bausch and Lomb Optical Company at Rochester, New York.

During the past fifteen years five alumni memberships have been granted.

DR. FRANZ EDUARD SUESS, professor of geology at the University of Vienna, celebrated his seventieth birthday on October 7.

PHILIP GEORGE LANG, JR., of Baltimore, engineer of bridges of the Baltimore and Ohio Railroad, was elected president of the American Welding Society at the recent New York meeting. Colonel G. F. Jenks, of the Ordnance Department, U. S. Army, was elected senior vice-president. The Samuel Wylie Miller Memorial Medal for "meritorious achievement contributing conspicuously to the advancement of the art of welding and cutting" was awarded to H. Sidney Smith, consulting engineer of the Union Carbide Company, New York.

AT Cornell University the title of professor emeritus has been conferred on Dr. Frederick Bedell, of the department of physics; on Dr. Wilder D. Bancroft, of the department of physical chemistry, and on Professor Edgar H. Wood, of the School of Engineering.

PROFESSOR J. H. VAN VLECK, of Harvard University, has been appointed visiting professor at Princeton University for the first half of the present academic year.

DR. WILLIAM N. PARKINSON, since 1929 dean of the School of Medicine of Temple University, has been elected vice-president of the university.

IN the College of Applied Science at Syracuse University, Professor Cecil S. Camp, of the Mississippi State College, has been appointed assistant professor of civil engineering, and Dr. Charles D. Luke, of the De Florez Engineering Company of New York City, has been appointed assistant professor of chemical engineering.

PROFESSOR J. B. S. HALDANE has been appointed the first incumbent of the chair of biometry at University College, London. This chair was established in memory of W. F. R. Weldon, distinguished for his work on biometrics, by Mrs. Weldon, who bequeathed her residuary estate in trust for the foundation of "a professorship of biometry for the higher statistical study of biological problems."

DR. C. K. INGOLD, professor of organic chemistry at the University of London, has been made director of the chemical laboratories of the university. Dr. Ingold lectured at Stanford University during the spring quarter.

DR. ALFRED KÜHN, of Göttingen, has been appointed professor of zoology and comparative anatomy at the University of Berlin.

The following specialists have been appointed incumbents of the Multiple Industrial Fellowship recently established at Mellon Institute by the Cotton Research Foundation: D. M. Musser, who received the Ph.D. degree last June from the University of Wisconsin; Dr. R. F. Nickerson, formerly physical chemist at the Worcester, Mass., State Hospital, and Dr. H. S. Olcott, recently research associate in biochemistry at the University of Iowa. The work of this group is being guided by Dr. L. W. Bass, assistant director of the institute.

DR. G. E. F. LUNDELL, assistant chief of the Division of Chemistry of the National Bureau of Standards, has been appointed chief to fill the vacancy caused by the retirement of Percy H. Walker. Dr. Lundell will be succeeded as assistant chief of the division by Dr. C. E. Waters, who has for many years been in charge of the section on organic chemistry.

G. E. ALTSTATT, plant pathologist, has been made acting chief of the Division of Plant Pathology and Physiology of the Texas Agricultural Experiment Station during the illness of Dr. J. J. Taubenhaus, who is now convalescent.

DR. CHARLES HOWE ELLER, Richmond, director of the bureau of rural health of the Virginia State Department of Health, has been appointed health officer of the Eastern Health District in Baltimore. He succeeds Dr. Harry S. Mustard, who resigned to become Hermann M. Biggs professor of preventive medicine in the New York University College of Medicine.

DR. ROBERT CUSHMAN MURPHY, curator of oceanic birds at the American Museum of Natural History, New York City, returned on October 12 from an expedition along the Pacific coast of Colombia from Panama to Guayaquil.

DR. PAUL WEISS, associate professor of zoology at the University of Chicago, has returned from a six months' leave in Europe, during which he gave lectures and engaged in research on the nervous system. He visited Belgium, Sweden, England, Germany, Switzerland, Austria and Holland.

DR. CARL J. WIGGERS, professor of physiology at the School of Medicine of Western Reserve University, has returned from the Orient, where he delivered a series of sixteen lectures in Canton, Hong Kong, Shanghai, Peiping, Seoul, Kyoto and Tokyo. He plans to address the sixth National Congress of Medicine in Cordoba, Argentina, in October, 1938, the other guest speakers being Professor Gregorio Marañón from Madrid and Professor Volhard from Germany.

AT the U. S. Geological Survey A. A. Baker and M. N. Bramlette have completed this season's field

mapping of the geology in a part of the Strawberry Valley quadrangle, Utah County, Utah, an area containing deposits of oil shale, coal, oil, gas and phosphate; C. B. Hunt has completed another season's field study and detailed mapping of the structure, igneous rocks, mineral resources and physiography of the Henry Mountains, Utah; W. G. Pierce has returned to Washington, having spent five months continuing a study of the geologic structure and fuel resources on the west side of Big Horn Basin in Park County, Wyoming; A. H. Koschmann has completed field studies of the geology and ore deposits of the Cripple Creek district and the Chattanooga district near Silverton, Colo.; field studies in the LaPlata Mountains, southwestern Colorado, conducted in cooperation with the State of Colorado, have been completed by E. B. Eckel and A. C. Spencer; W. H. Monroe is making a reconnaissance study of the Upper Cretaceous formations of Alabama with special attention to the correlation of these formations with those of Mississippi and Georgia.

PROFESSOR E. V. HUNTINGTON, of Harvard University, delivered two lectures during July at the third annual conference of the Cowles Commission for Research in Economics at Colorado Springs.

THE Dohme Lectures at the Johns Hopkins School of Medicine will be given on November 10, 11 and 12 by Einar Lundsgaard, professor of physiology at the Institute of Medical Physiology of the University of Copenhagen. The titles of the separate lectures are as follows: "The Chemistry of the Anaerobic Muscular Contraction," "The Metabolism of the Aerobic Working Muscles" and "The Metabolism of the Isolated Liver."

SIR HUMPHRY ROLLESTON gave the inaugural address at the opening on October 6 of the ninety-sixth session of the School of the Pharmaceutical Society of Great Britain.

THE autumn meeting of the National Academy of Sciences will open on October 25 at Rochester, New York. Members will be welcomed by Dr. Alan Valentine, president of the University of Rochester, and Dr. Frank R. Lillie, president of the academy, will respond. Sessions for the reading of scientific papers will be held on Monday and the two following days. In the afternoon of Monday members will be received at a tea given by President and Mrs. Valentine at Eastman House. The evening will be given over to a special concert at the Eastman Theater. On Tuesday visits to the Bausch and Lomb Optical Company and the Eastman Kodak Company have been arranged. At the subscription dinner in the evening Dr. E. O. Lawrence, of the University of California, will be presented with the Comstock Prize. The address at the dinner will be made by Arthur C. Parker, director of the Rochester Museum of Arts and Sciences, on "The Anthropologist Looks Ahead."

THE two hundred and sixteenth regular meeting of the American Physical Society will be held at the University of Chicago on November 26 and 27. Other meetings for the current season are as follows: December 17 and 18, Stanford University; December 28 to 30, annual meeting, in conjunction with the American Association for the Advancement of Science, Indianapolis, Ind.; February, 1938, New York, N. Y.; April, 1938, Washington, D. C.

THE United States Civil Service Commission announces open competitive examinations on November 8 for the positions of associate geophysicist, at a salary of $3,200 a year, and assistant geophysicist, at a salary of $2,600 a year. At present a vacancy in the position of associate geophysicist exists in the U. S. Geological Survey. Competitors will not be required to report for examination at any place, but will be rated on their education and experience, such ratings being based upon candidates' sworn statements in their applications and upon corroborative evidence. An examination also will be held on November 8 for the position of cottonseed technologist at a salary of $3,800 a year. Full information can be obtained by addressing the commission at Washington, D. C.

THE Edward Martin Biological Laboratory of Swarthmore College was dedicated on October 2. President Aydelotte introduced as speakers Dr. Laurence Irving, as director of the laboratory; Dr. James Rowland Angell, as the principal speaker for the occasion, and Dr. Edward Martin, for whom the building was named. The building and endowment represent the gift of Fred M. Kirby to the college as a symbol of his friendship for Dr. Martin and to record his admiration for his devotion to public service, science and education. The building contains laboratories and equipment for teaching and research in biology and psychology.

A LUNCHEON of the Benjamin Franklin Memorial and the Franklin Institute was given on October 12 in the memorial chamber of the Franklin Institute, Philadelphia, to make public plans for the dedication of the Benjamin Franklin Memorial next spring, when the statue of Franklin will be placed in Franklin Hall. Representatives of the federal, state and municipal governments, as well as of foreign countries, will participate. At the luncheon Philip Staples, president of the Franklin Institute, outlined the plans and activities of the various committees and Dr. George Wharton Pepper, honorary chairman of the

Dedication Committee, presented a résumé of the project and explained the sponsorship of the erection of a national memorial to "Franklin—the Scientist, the Diplomat, the Printer, the Great American."

THE University of Colorado Museum is moving into its new building, which was finished about September 15 at a cost of $150,000. It was built with the cooperation of the Public Works Administration. There are four floors, two of which are for exhibitions, one for teaching, research and administration, and one for the housing of the study collections. There will be exhibits in biology, southwestern archeology, geology, mineralogy and paleontology. It is hoped that it will be possible to open the museum to the public about the middle of November. Professor Hugo G. Rodeck is curator.

DISCUSSION

A PSYCHIATRIC ANALYSIS OF THE PRESENT-DAY MADNESS IN THE WORLD

IT has often been stated that the world to-day is insane. When one looks upon the various nations racing madly toward the next war, toward the despotism that reigns over many countries, on the self-inflicted poverty, on the mad desire not to cooperate with others, it is not strange that the world may be regarded as mad.

Insanity, however, is a broad term which covers many different types of personalities and many different types of diseases. Even after a full study it is often impossible to come to a definite conclusion. Nevertheless, it is important to make a diagnosis because upon the diagnosis depends the therapy.

Such a diagnosis is submitted in the following analysis of the various countries. There are many difficulties, many objections and much conflicting evidence to the following statements, but they are submitted in an effort to arouse interest, to stimulate the ideas and the controversy that is necessary in order to throw light upon the events of the day. It is possible that there will be objections; that is too bad. An individual or country must be able to look at itself, to laugh at itself and to understand itself as it is. Whenever a country or an individual becomes too upset by criticism, then that person is basically unstable. The well-balanced man is not affected by criticism, except that it makes him reflect and take into consideration the objections which are offered to his personality. It is with this hope that the following statements are made.

The United States is suffering from a typical manic-depressive psychosis. In the manic phase, just as in the manic patient, it is happy, elated, very active, dreaming great dreams, doing many things beyond its capacity and speaking loudly of the success which it is achieving. Such a manic attack reached its climax in the years before 1929. Following the crash in 1929 came the depressive episode, and here again the analogy between this depression and the manic-depressive depression is striking. In both instances is there a marked retardation, marked ebbing of energy, many complaints, inability to think through clearly, insomnia, bad dreams, fears, a poor appetite and a decline in the birth rate. He needs to learn to smooth out his swings.

France reminds me of an elderly, fearful spinster, gingerly treading her way, holding her skirts high, suffering from an excessive emotionalism and apprehensiveness. She was born in the eighteenth century with violent labor pains and much hemorrhage. She is excessively dependent on her brother, John Bull. She is of basically good character but unstable, is brilliant but unreliable.

Germany is going through a depressive phase with marked paranoid symptoms. The depression has been chronic; the paranoid ideas have been coming on gradually in the last few years. She feels that other people are to blame for her own inadequacy. She accuses others with the typical rationalization used by paranoids for her inferior condition. She is, again like most paranoids, eminently logical. She is extremely capable and full of energy and, again like the paranoid patient, goes into meticulous and infinitesimal detail to prove that she is right in her accusations. Such persons are always potentially very dangerous, because they possess reason and great energy. It is hoped, however, that with the lifting of the depression the paranoid symptoms will tend to subside and trust in others will replace suspicion of others. Germany needs to learn to place less emphasis on intellect and to be more tolerant of human emotions and errors.

Italy is really a feeble-minded person who has seen others grow great, who envies them and feels that he too can become a great person. The consequence has been much blowing of the horn, beatings upon the chest, large statements of the greatness of the individual, without any real intellectual attempt, or for that matter ability, to become important. In such instances a spanking often does good; on the other hand, it often leads to sulkiness. What is far more important for such a feeble-minded person is the need for his neighbors to put their foot down on anything that is wrong, while giving him great praise for what he does that is right, no matter how small.

Japan is a small, dynamic, psychopathic personality with marked temper outbursts and ideas of grandeur. Because of its basic characteristics it antagonizes

people and insists upon its own way. Such persons are motivated by a single idea and will often perish rather than give it up. It will be a long time before it will be content to govern just itself.

Russia is physically a strong young man who has just passed through the throes of puberty. There has been much internal conflict with emotional discord, unsettledness of purpose, vague ideals and dreams, reckless pursuit of a shadowy goal without much consideration to the practical obstacles. With the passing from the stage of puberty into the stage of adolescence it begins to develop more and more sense. It is still, however, far from leaving the impractical idealism of the youth. Age may give it wisdom.

China reminds me of a middle-aged, bald-headed man who once was very fat but now has become gaunt and has large hanging folds of skin. He is essentially lazy, calm, philosophical, and would rather spend his days fishing than working in the field. He is a kindly old soul who wishes to be left alone and desires not to interfere with other people. There are some signs, however, of his becoming very irritable at the persistent stings given him by the irascible, small, psychopathic neighbor. He will lose his temper some day and chastise this neighbor. The irritation will make a man out of him, so that after getting rid of it, he will settle down to a more organized and systematized life.

England is a solid, settled business man who has just gone through a depression and has "taken it like a man." However, because of his age, near the sixties, he is conservative, somewhat apprehensive, wishes to let things take their course, and does not desire to interfere with the ordinary plan of things. He has a large background of experience, knew what it was to be the head of a large firm and still has many potentialities. It remains to be seen whether age will get the better of him. He has become "too set in his ways" and needs to change. He has many grown-up sons, some of whom are stable, some of whom are unstable, but practically all of whom are wilful. These colonies take after their parent in some ways.

The only really normal countries in this world to-day are Norway, Sweden, Denmark, Holland and Switzerland.

Holland is a calm, placid, peaceful man of middle age who goes his own way, minding his own business, working industriously, taking care that his toes are not particularly stepped on, but free from any real hysteria.

Norway and Sweden similarly are hard-working, clean citizens who wish only to be let alone, to cooperate in the community singing group and to be allowed to earn an honest living.

Switzerland also is normal but quite uneasy because of his neighbors. There are signs of insomnia and general restlessness.

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RATE OF REACTION AND CONCENTRATION OF ENZYME

THE note by Dr. Oscar Bodansky in the July 16 issue of SCIENCE concerning the invalidity of the widely accepted "Schütz-Borissov Law" for the relation between rate of reaction and enzyme concentration recalled some work[1] on this subject by some colleagues and myself which seems to have been not at all noted by chemists. Dr. Bodansky points out that while the Schütz-Borissov law is to the effect that the velocity of reaction is proportional to the square root of the concentration, the velocity is actually proportional to the first power.

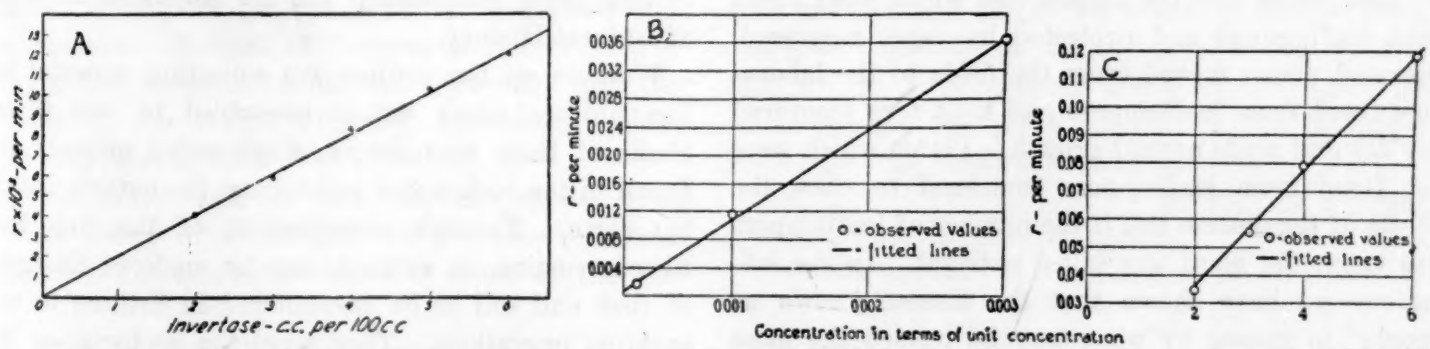

FIG. 1. A. Invertase and Sucrose (data from Nelson and Hitchcock, *Jour. Am. Chem. Soc.*, 43: 2632–55, 1921). B. Urea and Urease (data from Van Slyke and Cullen, *Jour. Biol. Chem.*, 19: 141, 1914). C. Dipeptid and Enzyme (data from Abderhalden and Michaelis, *Zeits. Physiol. Chem.*, 52: 326, 1907).

Our work was concerned primarily with the testing of a proposed equation for describing the course of the reaction between enzyme and substrate. One of the parameters of the equation measures the rate of reaction, and incidental to our work we studied the relation of the rate so measured to the enzyme concentration. Our results clearly support Dr. Bodansky's

[1] J. Berkson and L. B. Flexner, *Jour. Gen. Phys.*, 11: 433, 1928. J. Berkson and F. Hollander, *Jour. Wash. Acad. Sci.*, 20: 157, 1930.

contention that the relation is linear. This can be shown graphically, as illustrated in Fig. 1.

MAYO CLINIC JOSEPH BERKSON
ROCHESTER, MINN.

PEANUT "POUTS"

MANY years ago my attention was called to a condition of peanut plants which resembles very closely a condition known in potatoes as tipburn. Associated with the peanut plants showing this condition was the common potato or bean leafhopper (*Empoasca fabae* Harris). At that time I surmised that this disease was similar to potato tipburn and was caused by the leafhopper. Other duties prevented any more work on the problem until last year. This past season, laboratory and field experiments have proven beyond a doubt that the disease which is known locally as "pouts" is caused by the common potato or bean leafhopper. This disease appears first as a distinct blackish discoloration at the tip of the leaflet, and the discoloration progresses gradually toward the base of the leaflet until the whole leaflet is involved. If the disease is severe, the entire leaf turns blackish, shrivels and dies. Typically, in the field, the plants recover about blooming time and there is no further evidence of the disease. At this time also, the leafhoppers disappear from the peanut field and seem to migrate to the fields of soy-beans. Although we have not as yet been able to prove this migration in the field, all the evidence points in that direction.

In the field plants which were protected from the leaf-hoppers the disease did not develop, whereas unprotected plants did develop the disease. Plants in the field which had the disease and which were freed from leafhoppers and protected by cages recovered. Diseased plants moved from the fields to the laboratory freed from leafhoppers and kept free recovered rapidly and made normal growth. Plants which were not freed from leafhoppers continued to show the effects of the disease and if the number of leafhoppers was large, the plant was killed outright. In the laboratory we have shown that the disease known as "pouts" is caused by what may be termed the mass effect of toxins. In the laboratory small plants, with two leaves, which were in good growing condition and which were stimulated by plant food and frequent waterings were able to outgrow the effects of one or two leafhoppers per plant. Those, however, which had three or more leafhoppers per plant did not recover and were killed, thus showing the mass effect.

The name "pouts" was given to this disease by the farmers because they said the peanut plant was "pouting" and after it commenced to bloom, it ceased to "pout." The name is, therefore, very appropriate and should be used to designate this condition of the peanut plant.

Thus we add to the long list of the host plants of this leafhopper still another important economic crop, for it has been shown in the past or experiments are now in progress which indicate that this insect is an important pest of alfalfa, clover, garden beans, soy-beans, beets, potatoes, cotton and peanuts.

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DATA ON FORAMINIFERA COLLECTED BY THE WORKS PROGRESS ADMINISTRATION

DATA on more than 15,000 genera and species of foraminifera, including 45,000 illustrations, are to be available for the information of geologists, engineers and other scientists as a result of work now being done by the Geological Research Project of the Works Progress Administration in New York City. Substantial progress toward the completion of the gigantic task of assembling this material has been reported to the Washington, D. C., office of the Division of Women's and Professional Projects of the Works Progress Administration. Ellen S. Woodward, assistant WPA administrator, is director of this division.

Results of the project are expected to be of material benefit to geologists, to the mining and petroleum industries and to those engaged in city planning, in agriculture and in the control and development of waterways. The project's manuscript has already been used in connection with the solution of problems in rock layer relationship for the American Museum of Natural History.

Workers on the project are collecting material on foraminifera never before assembled in one place. Shells of these microscopic, single-celled animals are found in the rock layers making up the outer crust of the earth. Through identification of the tiny fossilized remains, an estimate can be made of the type of rock and soil to be encountered in drilling or excavating operations. They serve the geologist or the engineer as the x-ray serves the surgeon.

In both the pure science of geology and its various applied forms, one of the most important considerations is the age of the different rock layers and their arrangement in relation to each other. Of the several ways in which ages and relationships can be determined by far the most accurate method is by means of animal remains embedded in the rocks. These animals lived in the ancient seas during the geologic age in which the particular rock layers were formed. Certain species of fossils occur in rock layers of a particular age, regardless of the geographic location of the rock formations. By identifying the animal re-

mains of a rock layer, its age and its relationship to surrounding layers may be determined.

The foraminifera are especially valuable in making such determinations. They are widely distributed; they have lived in great numbers since early geologic times; and many species are sharply restricted to rock formations of certain definite periods.

Although geologists have been accumulating data on foraminifera for more than two hundred years, this material has never been presented in a systematized form. A vast amount of unorganized data exists in geological libraries throughout the world. But only in large cities, such as New York, London or Rome, is there anything approaching a comprehensive collection of material. Even these collections are of little use to the research worker, as they are in chaotic condition.

It is the task of the Geological Research Project to collect and orientate material on foraminifera so that for the first time it may be presented to the scientific world in usable form for ready reference. The finished product will consist of at least twenty-five volumes of about 1,000 pages each, containing in all approximately 45,000 illustrations and bound in loose-leaf form so that supplementary material may be added to keep the work up to date.

The vision that made the project possible must be credited to Dr. Brooks F. Ellis, geologist of note, who more than ten years ago started unaided the long and difficult task. In 1930 he joined the faculty of New York University and subsequently secured the help of student assistants. Later he was aided by workers from the Emergency Work Bureau and the Civil Works Administration. New York University and the American Museum of Natural History agreed to supply the necessary literature. Finally, with the creation of the Works Progress Administration, the enterprise was made a WPA project.

As the WPA staff has been carefully selected from a large group of applicants, all are especially well qualified. The linguistic ability of some of the personnel is astonishing. One man has a thorough knowledge of ten modern languages as well as Greek and Latin. Many hold masters' degrees, while several have Ph.D. degrees in science. The roll of American and foreign universities represented is a long one.

Several prominent scientists who are familiar with the work of the project have declared that the results will have a vital and stimulating bearing upon the work of scientists in this field the world over.

As for practical results, since foraminifera constitute an excellent index to sub-surface conditions, the problem of water supply and the control and development of the waterways of the country will be more easily solved. The mining and petroleum industries will be aided directly and materially by the results achieved by this project.

At present the petroleum industry, according to experts' reports, is losing millions of dollars every year through unscientific methods of prospecting and developing. The present compilation will not solve all the difficulties encountered, but its application will greatly lessen the element of chance and will be of very great value to the federal and state governments in regulating and developing the production of petroleum.

Also, through the improvement in geologic and stratigraphic methods which this compilation will bring about, many related fields, such as agriculture and irrigation, will be materially benefitted.

Records on foraminifera have been used extensively in engineering work in and about New York City. City geologists have found them invaluable in developing the engineering and geologic background of such undertakings as the water supply system, bridge and pier foundations, the mid-town tunnel and certain harbor developments. These experts agree that on completion the WPA compilation will be put to immediate and productive local use.

A. W. VON STRUVE
WORKS PROGRESS ADMINISTRATION,
WASHINGTON, D. C.

QUOTATIONS

SCIENCE AND DEMOCRACY

SCIENCE as we know it is the child of democracy. Freedom of thought and of expression is the essence of both—a heritage from the British and French revolutions. That freedom is in peril. In none of the totalitarian states may an authority in any branch of science utter theories that conflict with the views of the ruling dictator on man's place in nature, society or the laboratory. Organized British science is alarmed. But not sufficiently alarmed, in the opinion of Ritchie Calder, a well-known journalist of London. He addresses an open letter to Lord Rayleigh, president of the British Association for the Advancement of Science, and demands an active cooperative participation of scientists all over the world in solving the problems that confront society.

To most of us science means medicine, and hence better health; observatories, and hence more knowledge about the stars; agricultural experiment stations, and hence better plants and animals; chemical laboratories, and hence compounds that outdo nature's. It stands for much more. Its triumphs are impossible

without perfect objectivity, a separation of hopes and desires from the things studied. It is primarily an attitude, perhaps the most important mental acquisition of man. Because of this attitude it is democratic. It knows no creed, no country. It achieves the only true internationality the world has ever known and thereby presents striking evidence that men can sink their differences of opinion and their passions and work for a common cause.

The salvation of this international democracy of science and of this objectivity, as Mr. Calder and others see it, lies in a world-wide organization. He suggests that the British and American Associations unite to make the force of massed scientific thinking felt throughout the world. The first step would be the drafting of "a Magna Charta, a Declaration of Independence, proclaiming that freedom of research and of exchange of knowledge is essential, that science seeks the common good of all mankind, that 'national science' is a contradiction in terms." Even before this ringing appeal was addressed to Lord Rayleigh the more energetic spirits in England had started a movement to unite the British and American Associations for the purpose of combating the infectious bigotry that afflicts much of Europe. The British Association now discusses at its annual meetings the part that science can play in pointing out the course that society should follow if it would march on. This year its council took the initiative in "showing the nations of the world that they are members of a great commonwealth and in furthering the cause of international peace." To prove that these are not hollow words a deputation under Lord Rutherford is to convene with the Indian Science Congress and set an example of international action and solidarity.

Mr. Calder has not exaggerated. To save science his "World Association" is needed, an organization which shall indicate how the objective attitude of the laboratory may be applied in governing a people, in breaking down prejudices, in preventing war, in solving problems that mean progress not in one country alone but the world over. Will the American Association heed the appeal of its British counterpart? There was never a time when science had so vital a message to deliver, so high a social mission to perform.—*The New York Times.*

REPORTS

RESEARCH AWARDS OF YALE UNIVERSITY SCHOOL OF MEDICINE

FORTY-ONE awards, amounting to $28,263, have been assigned to members of the Yale teaching and research staffs under the provisions of the George H. Knight Memorial Fund and the Fluid Research Fund. These grants are made annually to aid in defraying the expenses of special investigations during the coming academic year. Awards have been made as follows for 1937–38:

Edgar Allen, professor of anatomy, to continue studies of the effects of sex hormones in small animals.

Henry G. Barbour, research associate in pharmacology and toxicology, for a continuation of investigations of the biological effects of heavy water in mammals.

Robert W. Clarke, instructor in physiology, for a study of renal clearance in monkeys.

George R. Cowgill, associate professor of physiological chemistry, for the following investigations: (1) joint research with Drs. Hoff and Nahum on the heart in vitamin B deficiency; (2) an extension of the work with the plasmapheresis technique on the effect of dietary factors on the regeneration of blood hemoglobin and blood cell stroma; (3) the relation of heightened metabolism due to hyperthyroid activity and other factors to the body's quantitative need for various dietary factors, particularly vitamins.

Daniel C. Darrow, assistant professor of pediatrics, for (1) a study of distribution of water and electrolyte in adrenal insufficiency; (2) a study of the distribution of water and electrolyte in convulsions.

Clyde L. Deming, clinical professor of urology, for a study of the anatomical origin of prostatic hypertrophy.

J. G. Dusser de Barenne, Sterling professor of physiology, for a continuation of studies on the physiology of the cerebral cortex and cerebellum in monkeys.

James C. Fox, clinical professor of neurology, and Donald G. Marquis, assistant professor of psychology, for studies of vibratory sensibility.

John F. Fulton, Sterling professor of physiology, for a continuation of studies of cerebral-cerebellar relationships in primates.

Arthur J. Geiger, instructor in medicine, Louis S. Goodman, instructor in pharmacology and toxicology, and Louis N. Claiborn, clinical instructor in surgery, for studies in pernicious anemia.

Edwin F. Gildea, associate professor of psychiatry and mental hygiene, for studies of lipoids in relation to disorders of the nervous system.

Alfred Z. Gilman, assistant professor of pharmacology and toxicology, for a continuation of the study of the osmotic relations between blood and urine.

Robert T. Hill, instructor in anatomy, for a study of the physiological relations of male and female gonads, and their connections with the rest of the endocrine system.

David I. Hitchcock, associate professor of physiology, for technical assistance in connection with studies of the standardization of hydrogen ion determinations, and of the combination or other reactions of amino acids and proteins with acids, bases and salts.

Hebbel E. Hoff, assistant professor of physiology, and John F. Fulton, Sterling professor of physiology, for a study of the primate motor unit.

Hebbel E. Hoff, assistant professor of physiology, and Louis H. Nahum, research assistant in physiology, for studies of cardiac arrhythmias.

Marion E. Howard, instructor in medicine, for a continuation of (1) studies on lymphogranuloma inguinale, and (2) study of the virus of lymphocytic chorio-meningitis.

Carlyle F. Jacobsen, assistant professor of psychobiology, for a continuation of studies of relations of behavior to neural functions.

Ralph H. Jenkins, assistant clinical professor of urology, for a study of the germinal epithelium of the testicle in relation to the endocrines.

Margaret A. Kennard, assistant professor of physiology, and Delafield DuBois, research assistant in physiology, for a study of skin resistance after cortical lesion.

Margaret A. Kennard, assistant professor of physiology, for study of frontal lobe functions in monkeys.

John H. Lawrence, instructor in medicine, to continue study of the comparative effects of x-ray and neutrons on tumors in animals.

Gustaf E. Lindskog, assistant professor of surgery, for the following studies: (1) The effect of environmental temperatures on the subtidal lung volume; (2) the effect of lipoidal on the normal pericardium; (3) the effect of Roentgen rays on the normal lung and pleura (pathological and physiological changes).

Cyril N. H. Long, professor of physiological chemistry, for a continuation of investigations on the relation of pituitary and adrenal glands to carbohydrate metabolism.

Donald G. Marquis, assistant professor of psychology, for studies of the visual functions of the cortex, and for an investigation of the neurophysiological mechanism of the sympathetic nervous response in emotional situations.

Clyde S. Marshall, assistant professor of anatomy, for studies of the pyramidal system and of accessory motor pathways.

Ralph G. Meader, assistant professor of anatomy, for studies of the evolution of the optic system, together with an experimental analysis of the evolution of retinal projection.

Arthur H. Morse, professor of obstetrics and gynecology, and Gertrude van Wagenen, research assistant in obstetrics and gynecology, for studies relating to the processes of reproduction.

Chris H. Neuswanger, assistant clinical professor of urology, to continue study of methods of treating various diseases of the ureter.

Ashley W. Oughterson, associate professor of surgery, to continue experiments on the effect of tobacco on the vascular system, and for investigations relating to tumors.

John P. Peters, John Slade Ely professor of medicine, and assistants, for studies of metabolism.

Theodore C. Ruch, instructor in physiology, for a comparative study of the sensory tracts of the spinal cord in relation to the process of "corticalization" of sensory function.

Elizabeth R. B. Smith, honorary research fellow, and Paul K. Smith, research assistant in pharmacology and toxicology, to continue the study of thermodynamic properties of amino acids and related substances.

Leon S. Stone, associate professor of anatomy, to continue and extend investigations dealing with studies of living nervous tissues in amphibian embryos.

Robert Tennant, assistant professor of pathology and surgery, and Averill A. Liebow, research assistant in pathology, for a study of growth characteristics of mammalian neoplasms by tissue.

Herbert Thoms, associate professor of obstetrics and gynecology, for a continuation of the study of physical constitution in relation to labor and pelvic types.

James D. Trask, associate professor of pediatrics, (1) to continue hemolytic streptococci studies; and (2) for clinical application of Goodpasture's method for the cultivation of virus on the chorio-allantoic membrane of the chicken egg.

George Valley, assistant professor of bacteriology, to continue the study of *Clostridium histolyticum*.

Abraham White, assistant professor of physiological chemistry, for studies on (1) the constitution of insulin and (2) sulfur metabolism.

Arthur M. Yudkin, clinical professor of ophthalmology, to continue studies on cataracts.

Harry M. Zimmerman, associate professor of pathology, for studies on convulsive disorders.

SPECIAL ARTICLES

A PROLONGED AFTER EFFECT FROM ELECTRICAL STIMULATION OF THE CEREBELLAR CORTEX IN UNANESTHETIZED CATS[1]

HAVING developed a technique which allowed permanent electrodes to be implanted on the cerebral cortex,[2] it was decided to try the effect of stimulation with this type of electrode on the cerebellum of unanesthetized animals with intact brains. The results obtained were so significant in the light of previous reports[3, 4, 5] that it was thought worth while to describe the main phenomena in a preliminary account.

The electrode consists of a stainless steel tube, containing an insulated silver wire, which is screwed into

[1] This work has been aided by a grant to Vanderbilt University School of Medicine from the Division of Medical Sciences of the Rockefeller Foundation.

[2] Sam L. Clark and James W. Ward, *Arch. Neur. and Psychiat.* (to be published).

[3] A. T. Mussen, *Brain*, 50: 313, 1927; *Arch. Neur. and Psychiat.*, 23: 411, 1930 and 25: 702, 1931.

[4] W. K. Hare, H. W. Magoun and S. W. Ranson, *Am. Jour. Physiol.*, 117: 261, 1936.

[5] H. W. Magoun, W. K. Hare and S. W. Ranson, *Arch. Neur. and Psychiat.*, 37: 1237, 1937.

a trephine hole in the skull. The end of the silver wire (embedded in a glass rod) which is in contact with the brain through a hole in the dura mater is the stigmatic electrode, the steel tube acting as the indifferent electrode. The voltage of the stimulating current is controlled through a volt-meter and the length of stimulus is determined by a timing device. The cats are unrestrained throughout the experiment.

The results of stimulation depend upon the strength of the stimulus and the location of the electrode, but when a sufficiently strong stimulus is used (2 to 5 volts 60-cycle sine wave current for 2 to 10 seconds) provided the animal has not been subjected to strong stimulation too recently, a series of movements lasting several minutes occurs which involves the various portions of the animal in a definite order. Stimuli of less strength produce briefer and less extensive effects.

The attack is quite different from the epileptic fits provoked by stimulation of the cerebral cortex; the movements are not so spasmodic and resemble somewhat the movements observed in "slow motion" pictures.

The results can best be presented by describing a single attack. In cat 59, for example, on May 5, an electrode was planted on the left side of the cerebellum at the margin of the vermis on the second folium back of the fissura prima. On May 10 a stimulus of 3.1 volts for 5 seconds produced the following results:

During the stimulus the cat suddenly drew back its head, leaving both fore feet extended in front. As the stimulus ceased, the cat lifted its left forefoot and held it up for 30 seconds. At 1 minute after the stimulus the left forefoot was again lifted gradually until it was held high in flexion. The foot and leg seemed sensitive to touch. The foot was gradually returned to the table but remained tense. At 1 minute 50 seconds after the stimulus the cat turned its head to the right and the right forefoot began lifting and appeared hypersensitive. After a short while this foot was replaced and the cat remained inactive until 4½ minutes after the stimulus, when the left hind limb began lifting and was held up. At 5 minutes the tail curved around to the right side and was held in this position while the cat turned in a small circle to the left. At 5 minutes 15 seconds the right hind limb began lifting and was held up awhile and at 5 minutes 30 seconds the tail curved tonically to the left, where it was held until 6 minutes 50 seconds. By 7 minutes after the stimulus the cat had apparently recovered.

While this attack is typical in that it shows the sequence of limb involvement, *i.e.*, homolateral then contralateral fore limb, followed by hind limbs in the same order, it does not present all the effects seen on head and trunk. When the cerebellum is stimulated on the right side (as was done in this animal with another electrode planted later) the same sequence occurs, beginning with the right (homolateral) fore limb. When the electrode is planted as near the midline as possible, on stimulation both fore limbs are involved at once and the cat may sit on its haunches with both fore limbs in the air; then both hind limbs become affected, so that the cat may try to raise both at once and teeter on its fore limbs as on a fulcrum, the tail meanwhile being held straight up. Since it is difficult to plant an electrode exactly in the mid-line, the limbs on one side may lead slightly in the parade of events.

The response usually begins with phases similar to those described by Hare, Magoun and Ranson[4]; at first, movements coincidental with the stimulus, followed by movements of opposite nature, appearing as a rebound. This may resemble the "tegmental reaction." Then, appearing over the space of 5 to 10 or more minutes, the series of effects on the head, trunk, limbs and tail described above occur. In a few instances, near the termination of the first series, a new one has started with lifting of the homolateral fore leg, but as yet a second series has not continued through.

The pattern of the response varies with the location of the electrode on the cerebellum and while some 16 electrodes have been planted, much of the surface of the cerebellum is relatively inaccessible and has not yet been explored with this method. While the response begins according to the particular spot stimulated, the events occurring throughout the long after effect seem to suggest that other parts (perhaps all) of the cerebellar cortex, are gradually involved.

The pattern of response is a constant one for each point under controlled conditions, just as was the case with the cerebrum. Similar factors seem to influence responses from the cerebellum and cerebrum, since anesthesia and previous strong stimuli diminish the response to stimuli in both; weaker stimuli produce the beginning of the pattern or a proportional amount of it. Various operative procedures have been carried out to determine the effect on these attacks, and these will be discussed later in detail, but it is interesting that the long sequence of events resulting from stimulation was not abolished by removal of the contralateral motor area of the cerebrum in 2 cats nor by splitting sagitally the cerebellum in one cat. (At autopsy it was found that the cerebellum was successfully split except in the periphery of the vermis both anteriorly and posteriorly.) In two cats when a lateral lobe of the cerebellum was removed and the intact half stimulated, the long after effect involved only the homolateral fore limb.

The results of this work promise support in general for a localization of cerebellar cortical areas as de-

ribed by Mussen,[3] though details are yet to be orked out.

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CRYSTALLINE PAPAIN[1]

CRYSTALS showing proteolytic activity have been olated from the undried latex of green papaya fruit. he crystals show the usual properties of proteins. he substance contains nitrogen precipitated from queous solution by trichloracetic acid and has been olated by methods commonly employed in the purifi- tion of protein.

The crystalline material clots milk, digests casein nd splits hippurylamide in the presence of added ysteine under the conditions usually employed for emonstrating the activity of papain. The activity f the crystalline preparation per mg of protein nitro- en as measured by milk clotting or by casein digestion from 25 to 50 per cent. higher than that of any f the amorphous preparations made in this labora- ry, and is about twice as great as that of the best ommercial preparations.

No essential difference in activity was observed etween thrice and five times crystallized material, nd the ratio of the milk-clotting, casein-digesting and ippurylamide-splitting properties is approximately he same as found in dried latex and in amorphous recipitates prepared from fresh latex.

Without added activator, the activity of the crystals aries, apparently depending upon the treatment dur- g preparation. Determinations made without added tivator are obviously not as accurate as those run the presence of cysteine, because of oxidation dur- g the time of digestion. Accordingly the values btained in short-time intervals (milk clotting data) re probably the most accurate. On this basis some of he crystals were nearly inactive, others showed origi- ally about half the maximum activity. All these reparations reached the same level of activity when re-treated with cysteine. A small sample of thrice ystallized material which was half active was incu- ated with dilute hydrogen peroxide and then crystal- zed three times more to remove the reagent. The nal crystals were between 94 to 97 per cent. inactive.

Due to lack of raw materials, the quantity of crys- ls available thus far has been extremely small, and any desirable experiments have had to be postponed ntil more material is available. Recently crystals ave also been obtained from commercial papain but ave not yet been freed from amorphous material.

Improvements in the method for preparing the ystals will also be studied. Those used presently ere prepared in outline as follows:

Coagulated papaya latex, preserved with toluene, was suspended in some cases in about four times its weight of water, in other cases in about two volumes of 0.25 saturated ammonium sulfate. After about an hour the material was filtered and the clear filtrate was made 0.6 to 0.7 saturated with ammonium sulfate and filtered. The semi-dry filter cake was suspended in about an equal weight of water. The pH was adjusted to light green to brom thymol blue and the solution was cooled slowly from 20° to 5° C. (24 hours). The solution containing about 15 mg protein nitrogen per cc became turbid on cooling and in a few days developed a sheen due to the formation of small needle crystals. Particularly after crystal formation, slow addition of a saturated solution of ammonium sulfate may increase the yield. Recrystallization was carried out by essentially the same technique.

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THE MECHANISM OF BACTERIOPHAGE PRODUCTION[1]

WHEN bacteriophage is added to a culture of susceptible bacteria growing in an appropriate medium two phenomena occur. First, during the period of contact there is produced a considerable additional amount of phage and, second, as a terminal event the bacteria quite suddenly break up, leaving the medium clear.

d'Herelle[2] and Burnet[3] have stressed the importance of cellular lysis in the production of phage. According to them phage particles penetrate into the bacterium, multiply, but remain under spatial constraint until set free when the cell undergoes dissolution. Sufficient experimental evidence has accumulated to prove that bacterial lysis is not causally related to the phage-producing mechanism.[4] In the place of lysis, bacterial growth has come to be considered a *sine qua non* for phage production. Krueger and Northrop[5] found that factors such as reduced temperature or limitation of nutrients, which interfere with bacterial growth, likewise reduce phage formation. They de-

[1] The experimental work cited in this paper was supported by grants-in-aid from the National Research Council, the American Medical Association and the Board of Research, University of California.

[2] F. d'Herelle, "The Bacteriophage and Its Behavior." Williams and Wilkins Co., 1926.

[3] F. M. Burnet, *Brit. Jour. Exp. Path.*, 10: 109, 1929.

[4] A. P. Krueger, *Physiol. Reviews*, 16: 1, 1936.

[5] A. P. Krueger and J. H. Northrop, *Jour. Gen. Physiol.*, 14: 223, 1930.

[1] Food Research Division contribution No. 343.

veloped a differential equation expressing the rate of phage production in terms of the rate of bacterial growth and from it derived integral forms satisfactorily predicting the time of lysis, concentrations of bacteria at the moment lysis begins, etc.

More recently Scribner and Krueger,[6] investigating the kinetics of the phage-bacterium reaction in the presence of 0.25 N. NaCl, demonstrated that just before lysis there is a period of some 0.7 hour during which phage production continues, although the bacterial population remains stationary. Additional experiments reported by Krueger and Fong[7] indicate that such dissociation of bacterial growth and phage formation can be accomplished under different circumstances even in the absence of increased salt concentrations. By adjusting the pH and temperature, the bacterial substrate can be maintained in the resting phage, *i.e.*, without growth, while phage formation continues at the rate of a tenfold increase per hour.

The selection of bacterial growth as the essential conditioning factor for phage production and the use of bacterial growth data in deriving the equation for the kinetics of the phage-bacterium reaction were then merely fortuitous and, as shown here, without significance in defining the mechanism. The expression for bacterial growth should be replaced by the terms of some other reaction proceeding logarithmically with time as the growth does, and paralleling growth quite closely in the conditions requisite for its operation.

There is good reason to believe that phage is a protein with the properties of an enzyme,[4, 8] and the experiments cited above show that the mechanism of phage production can be studied like any other cellular mechanism of enzyme formation under conditions which set it apart from the complexities of cellular growth.

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PURIFICATION OF TOBACCO MOSAIC VIRUS AND PRODUCTION OF MESOMORPHIC FIBERS BY TREATMENT WITH TRYPSIN

TREATMENT of impure tobacco mosaic and other virus solutions with trypsin has been stated[1] to facilitate purification of the virus proteins. The proteins were later isolated as liquid crystalline concentrates, but it was not indicated whether trypsin aided isolation in the usual crystalline forms. Pure virus protein is not digested at a measurable rate by any proteolytic enzyme yet tried.[1, 2] Preparations of crude virus protein of tobacco common mosaic, which had received very little preliminary treatment and could not be crystallized by any of the usual methods, yielded pure protein readily after incubation with trypsin. The purified protein separated first in long mesomorphic fibers at pH 7.5, and crystallized in the typical needle form immediately upon acidification to pH 4.5.

In a typical experiment, the impure virus protein in approximately 1 per cent. solution, was incubated for 3 to 5 hours with 3.3 mg/cc of Fairchild's trypsin. The protein precipitable by trichloroacetic acid decreased in a few minutes from 11.4 mg to 8.3 mg/cc, and in a few hours the solution assumed an opaque appearance. Apparently pure virus protein had separated at pH 7.5, in a form readily identified microscopically as that described recently by Best[3] as mesomorphic fibers of virus. Shaking the solution disintegrated the fibers. The liquid was thereafter opalescent, but quite clear. On standing an hour or two the satin-like opaque appearance of the solution returned and the fibers had reformed. Acidifying the solution to pH 5 precipitated excellent crystals of the typical needle form of the protein, which were readily recrystallized.

Lojkin and Vinson[4] and Ross[5] have reported that purified solutions of virus incubated with Fairchild's trypsin are not infectious, but become so after heating to 70°. Assays were made of the virus protein purified by incubation with trypsin and subsequently crystallized, and also of virus crystals obtained in the usual way (referred to as the controls). All samples were brought to an equivalent protein content, 5.8 mg/cc, in 0.1 M phosphate buffer at pH 7; they were then diluted at suitable steps in the same buffer and used to inoculate the first leaves of 8-day old bean plants, *Phaseolus vulgaris* L., variety Scotia.

TABLE 1

	Dilutions		
	10^{-3}	10^{-4}	10^{-5}
Control*	300.2‡	19.3	5.40
Trypsin treated	215.4‡	32.3	8.26
Control*	....	46.1§	...
Trypsin treated	....	54.3§	...
Control†	....	97.3¶	...
Trypsin treated	....	164.6¶	...

* Crystalline virus stored in pH 7 buffer.
† Crystals stored under 0.5 saturated ammonium sulfate.
‡ Average number of lesions per plant on 15 plants.
§ " " " " " " " 10 "
¶ " " " " " " " 100 "

[6] J. Scribner and A. P. Krueger, *Jour. Gen. Physiol.*, 21: 1, 1937.
[7] A. P. Krueger and J. Fong, *Jour. Gen. Physiol.*, 21: 2, 1937.
[8] J. H. Northrop, SCIENCE, 84: 90, 1936.
[1] F. C. Bawden, *et al.*, *Nature*, 138: 1051, December 19, 1936.
[2] F. C. Bawden and Pirie, *Nature*, 139: 546, March 27, 1937.
[3] R. J. Best, *Nature*, 139: 628, April 10, 1937.
[4] M. Lojkin and C. G. Vinson, *Cont. Boyce Thomp. Inst.*, 3: 147, 1931.
[5] A. F. Ross (Abstract), *Phytopath.*, 25: 33, 1935.

Although there is a high degree of variability in virus assay methods, it appears that the infectivity of the trypsin purified protein is as great or greater than that of the controls. The virus protein after treatment with trypsin had been precipitated by ammonium sulfate at pH 4.5–5.0, filtered on Celite, and recrystallized three times by Stanley's procedure,[6] using CaO for elution, and acetic acid in ammonium sulfate for crystallization. It is probable that this subsequent treatment freed the preparation of trypsin, which either has only a temporary inactivating effect,[5] or acts on cells of inoculated plants so as to prevent entry of virus into living cells, when it is still present in the inoculum.[7]

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CATALYTIC REDUCTION OF THE METHYL ESTER OF 2:3:4-TRIACETYL α-METHYL-GALACTURONIDE TO METHYL-GALACTOSIDE

IN a recent note[1] there was described the reduction of methyl ester of 2:3:4-trimethyl α-methyl-d-galacturonide to 2:3:4-trimethyl α-methyl-d-galactoside. We now wish to report on the reduction of the methyl ester of 2:3:4-triacetyl α-methyl-galacturonide to methyl-d-galactoside. Thus, in one step, reduction of the $-COOCH_3$ and deacetylation are accomplished.

The composition of the methylgalactoside was as follows: C 43.51, H 7.4, OCH_3 16.91 (for $C_7H_{14}O_6$ Calc. C 43.30, H 7.3, OCH_3 15.98).

The application of this method to the study of aldobionic acids and other uronic acid derivatives is in progress.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A METHOD FOR THE SECTIONING OF PROTOZOA EN MASSE

OF the methods commonly used for sectioning protozoa *en masse*, those of Sharp[1] (imbedding in a hard paraffin mold), Calkins[2] (entanglement in zooglea) and Belar[3] (glass tubing closed at one end by bolting cloth) are no doubt the most practicable. In an attempt to reduce the loss of specimens, the present method of imbedding in a bag made of mammalian mesentery was devised. I have used the method successfully in sectioning several lots of large endocommensal ciliates, and an account of the procedure may be useful to others.

To make a form over which the bag may be shaped, roll a bit of warmed hard paraffin of such size that a sphere 2 mm in diameter results; while still warm impale it on the end of a round wooden toothpick or on a wooden pin, pointed at both ends, about 5 cm long and 0.6 mm in diameter near the ends.

Excise a transparent piece of fresh mesentery (cat or rabbit) 1.5 cm in diameter, transfer it to a dish filled with warm salt solution to a depth of 7 cm and, after rinsing, dip it out with the paraffin head of the pin so that it hangs symmetrically over the head. Stick the pin head-upright into a piece of sheet cork and tie with fine, black, cotton thread (No. 80) an overhand knot securely around both mesentery and pin just below the head. Handling the pin by its cork base, plunge it head first into a deep dish of Bouin's fluid and shake it about head-downward in the fixative; the free edge of the bag can thus be made to stand out nearly at right angles to the pin and to harden in this position. Leave it immersed head-downward for 24 hours, allowing the cork to serve as a float.

Remove the pin from the cork, wash in 80 per cent. alcohol as usual, dehydrate and transfer to xylene for four hours to dissolve out the paraffin interior of the bag. Reimmerse in absolute alcohol, transfer to 80 per cent. for a day and with forceps push the bag off the pin. There results a tough, fairly rigid, thin-walled bag for receiving the protozoa; it has an opening equal to the diameter of the pin and has a draw string in place; it may be stored in alcohol until needed.

To get the fixed protozoa into the bag, transfer them to a watch glass of 80 per cent. alcohol. Make a small basket or low cylinder of fine-mesh wire gauze just large enough to receive the bag, immerse the basket completely in a watch glass of 95 per cent. alcohol and set the bag into the basket with its opening uppermost. With a pipette having a straight, slender tip about 2 cm long, transfer the protozoa to the bag under the dissecting binocular. They need merely to be released from the pipette directly above and near to the opening in the bag; they will drop or stream into it because of the greater specific gravity of the 80 per cent. alcohol. The process should not be

[6] W. M. Stanley, *Jour. Biol. Chem.*, 115: 673, 1936.
[7] W. M. Stanley, *Phytopath.*, 24: 1055, 1934.
[1] R. G. Sharp, *Univ. Calif. Publ. Zool.*, 13: 43, 1914.
[2] G. N. Calkins, *Jour. Exp. Zool.*, 27: 293, 1919.
[3] K. Belar, *Methodik der Wiss. Biol.*, 1: 735, 1928.
[1] SCIENCE, 86: 2232, 332, October 8, 1937.

hurried, for the successful transfer depends on the maintenance of an alcohol concentration of about 95 per cent. in and around the bag. Once inside, the top of the bag is drawn shut and the free ends of the thread are cut off near the knot. For greater security the overhand knot may be continued into a square knot before cutting off the ends. There is little danger of tearing the bag upon pulling it shut.

The entire bag plus contents is now to be dehydrated, cleared, infiltrated, imbedded and sectioned, though it is advisable to stain it in alcoholic eosin to facilitate orientation. Since the thread can not be sectioned, the section plane must be at right angles to the longitudinal axis of the bag. Begin cutting tangentially to the deepest part of the bag and proceed toward the thread.

If it is desirable to keep the protozoa concentrated in the bottom of the bag, a metal insect pin may be thrust through the free edges of the bag above the thread. With suitable wire supports at the ends of the pin, it may be kept in a horizontal position with the bag hanging downward from it throughout the entire procedure, including imbedding.

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THE PRESERVATION OF TETANUS TOXIN BY THE LYOPHILE PROCESS[1]

TETANUS toxin (tetanospasmin), obtained by drying the ammonium sulfate precipitate from a filtered broth culture, must be preserved under rigorous precautions. Aqueous solutions and stock bottles of powder which are repeatedly opened deteriorate rapidly. An additional difficulty is created by the actively hygroscopic behavior of the dried powder which causes errors in the weighing. MacConkey[2] recommended the use of a stable solution prepared by dissolving toxin in equal parts of pure neutral glycerine and distilled water. Most investigators consider it essential to perform guinea pig titrations of their stock toxin with each successive experiment. At the National Institute of Health in Washington, D. C., purified toxin, used as the basis for standardizing therapeutic antiserums, is preserved within small ampoules in vacuo under the influence of pentaphosphoric acid in a cold dark place.[3] The minimum lethal dose of this purified powdered material for 350 gram guinea pigs remains constantly at 0.006 mgm.

In an attempt to avoid these difficulties, the Flosdorf-Mudd lyophile technique[4] has been applied to the problem of tetanus toxin preservation. A known quantity of standard toxin, obtained from the National Institute of Health, was dissolved in distilled water and distributed in aliquot portions into a large number of small rubber-stoppered glass ampoules. The solutions were immediately frozen in a bath of dry ice and methyl cellosolve at −78° C., and then dried by high vacuum distillation from the frozen state. The containers were sealed individually under vacuum by heat fusion of the pyrex glass exhaust tubes, and stored away under ice refrigeration (8–10° C.). The powdery residue dissolved instantly when distilled water was reintroduced by syringe and needle through the rubber stopper, in contrast to the slow solubility of the original material.

For example, on one occasion a solution of standard government toxin, which had been obtained from the National Institute of Health, was distributed into 25 lyophile ampoules in 10 cc quantities. The original solution had been prepared in such fashion that, after processing, 0.8 mgm was left in each ampoule as a dry residue. On repeated titrations the MLD of this material was regularly found to be 0.008 mgm.

Five separate solutions of tetanus toxin have been processed by this technique. In each instance a slight inconstant diminution of the initial potency was observed, although within each batch of ampoules there was a consistent uniformity of titer as measured by the MLD test on guinea pigs. These solutions were of various strengths depending on the nature of the experiments in which they were to be used. This lyophile toxin has proved itself most dependable in the course of several series of experiments on tetanus intoxication and treatment carried on over a three year period. No single batch was used for longer than a one year period, however, since beginning deterioration was detected after that time.

In summary, therefore, the lyophile method of preserving tetanus toxin has been found a valuable and time-saving adjunct to experimental investigation.

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[1] Aided by a grant from the Eli Lilly Fellowship Fund.

[2] A. T. MacConkey, *Jour. Hyg.*, 22: 473–476, 1923–24.

[3] M. J. Rosenau and T. F. Anderson, *Hygienic Lab. Bull.* No. 43, March, 1908.

[4] E. W. Flosdorf and S. Mudd, *Jour. Immunol.*, 389–425, November, 1935.

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